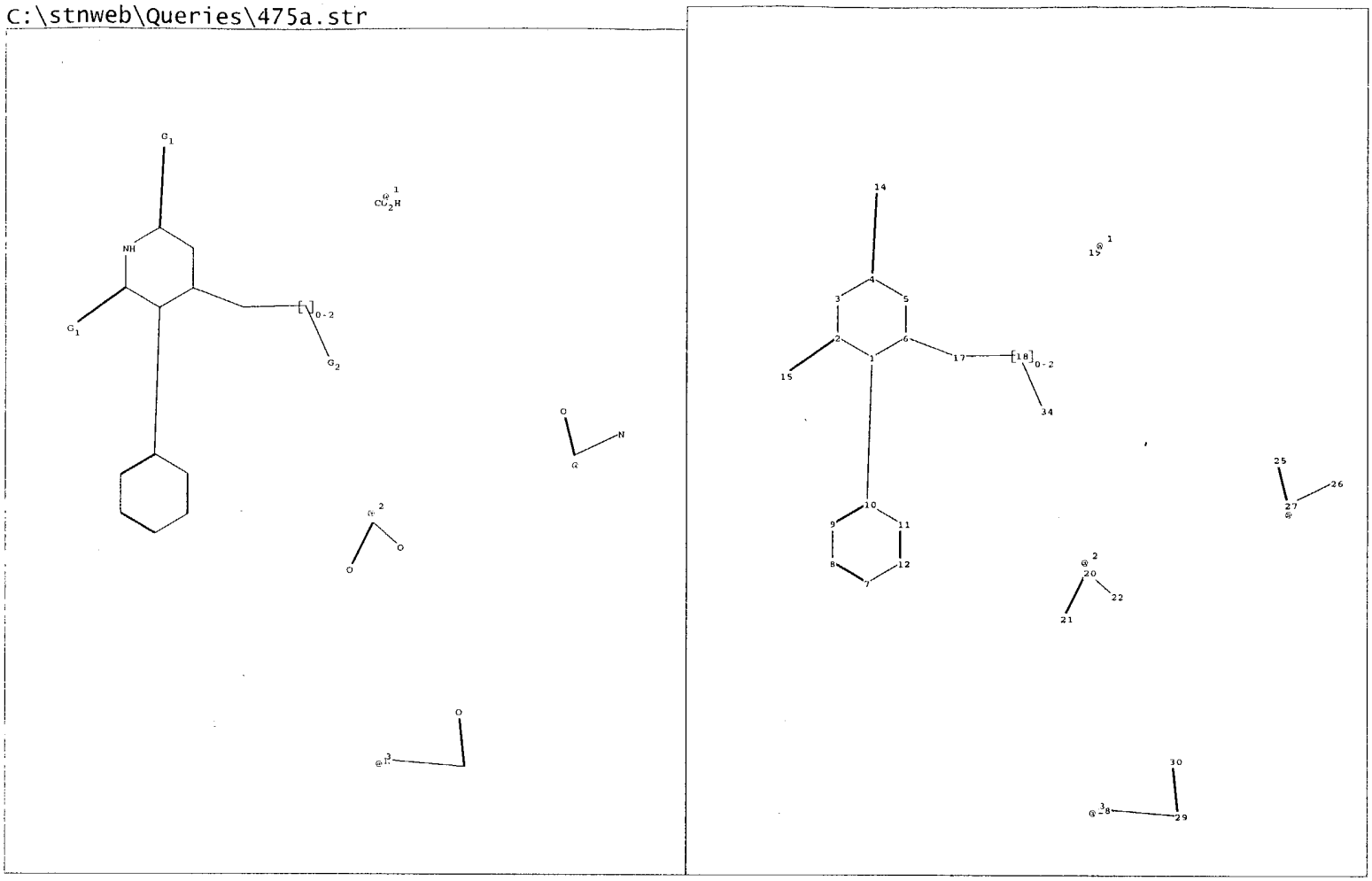
C:\stnweb\Queries\475a.str



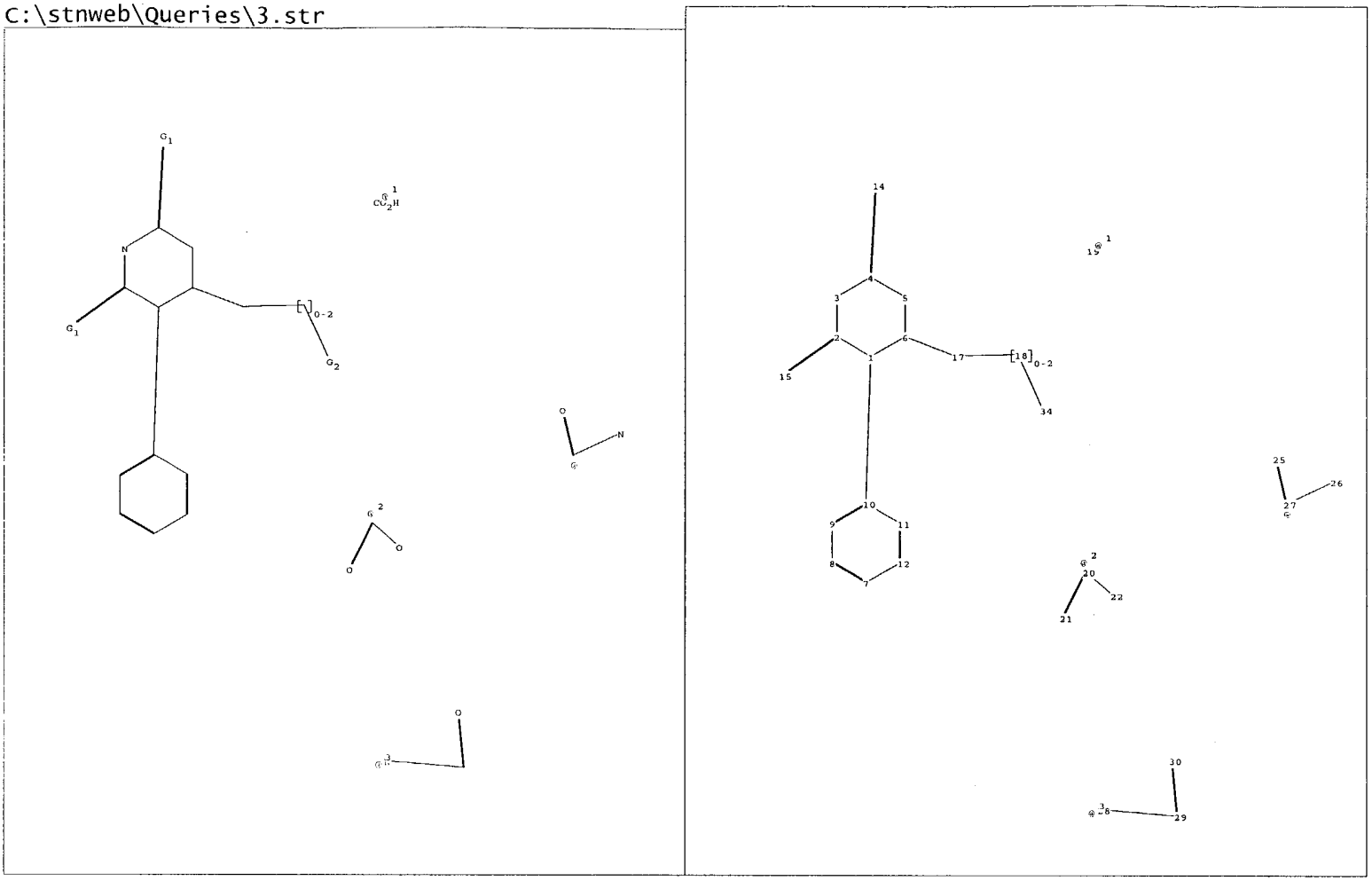
chain nodes :
14 15 17 18 19 20 21 22 25 26 27 28 29 30 34
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-10 2-15 4-14 6-17 17-18 18-34 20-21 20-22 25-27 26-27 28-29 29-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 2-3 2-15 3-4 4-5 4-14 5-6 18-34 20-21 20-22 25-27 26-27 28-29 29-30
exact bonds :
1-10 6-17 17-18
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 : 7 :

G1:O,S

G2:[*1],[*2],[*3]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 14:CLASS 15:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 34:CLASS

C:\stnweb\Queries\3.str



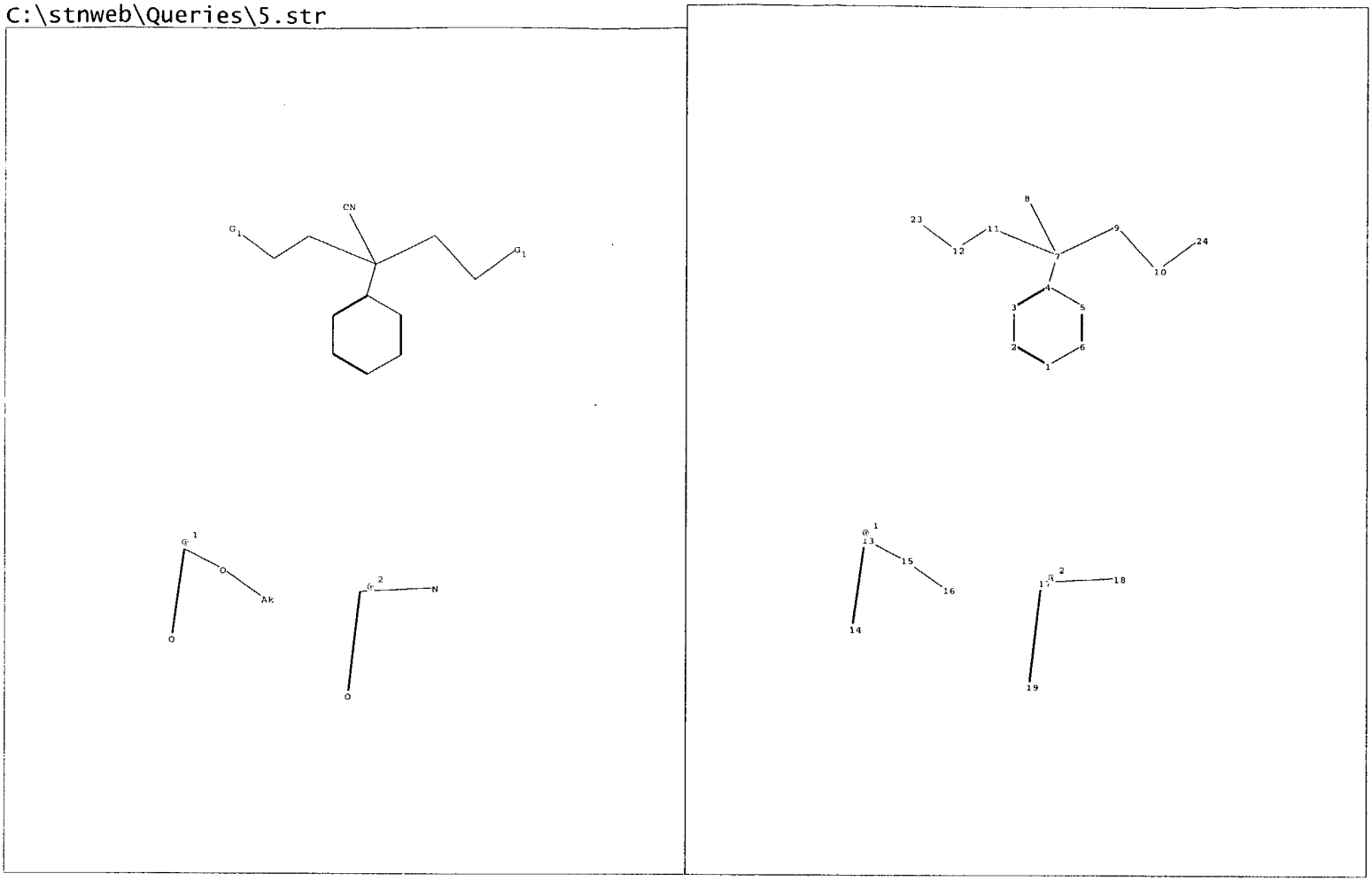
chain nodes :
14 15 17 18 19 20 21 22 25 26 27 28 29 30 34
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-10 2-15 4-14 6-17 17-18 18-34 20-21 20-22 25-27 26-27 28-29 29-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 2-3 2-15 3-4 4-5 4-14 5-6 18-34 20-21 20-22 25-27 26-27 28-29 29-30
exact bonds :
1-10 6-17 17-18
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 : 7 :

G1:O,S

G2:[*1],[*2],[*3]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 14:CLASS 15:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 34:CLASS

C:\stnweb\Queries\5.str

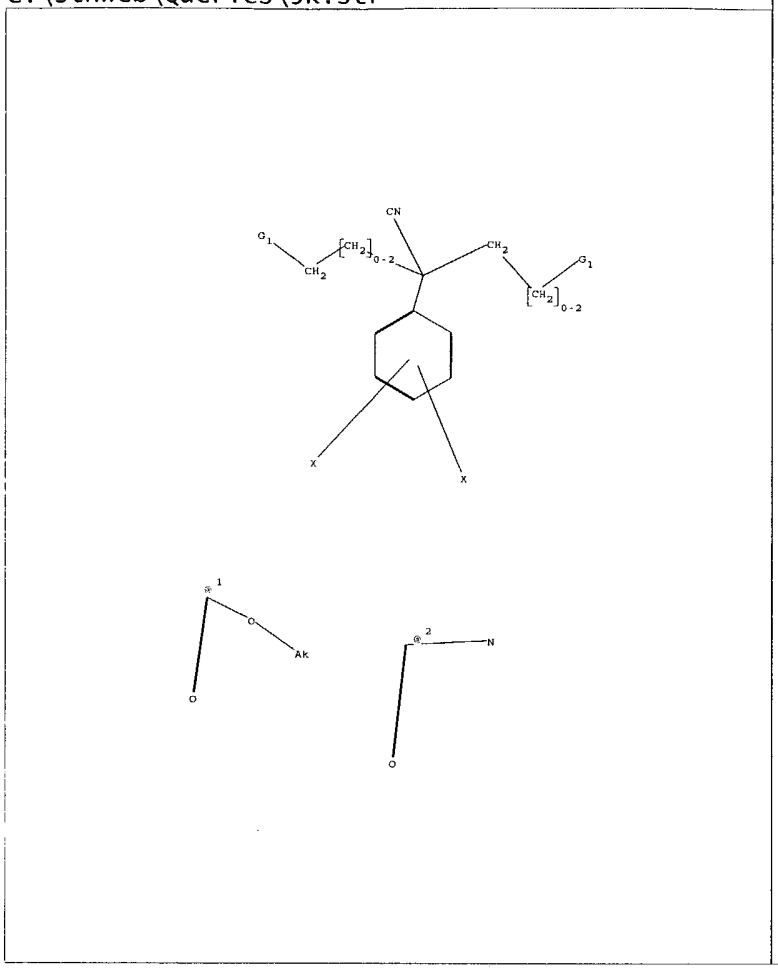


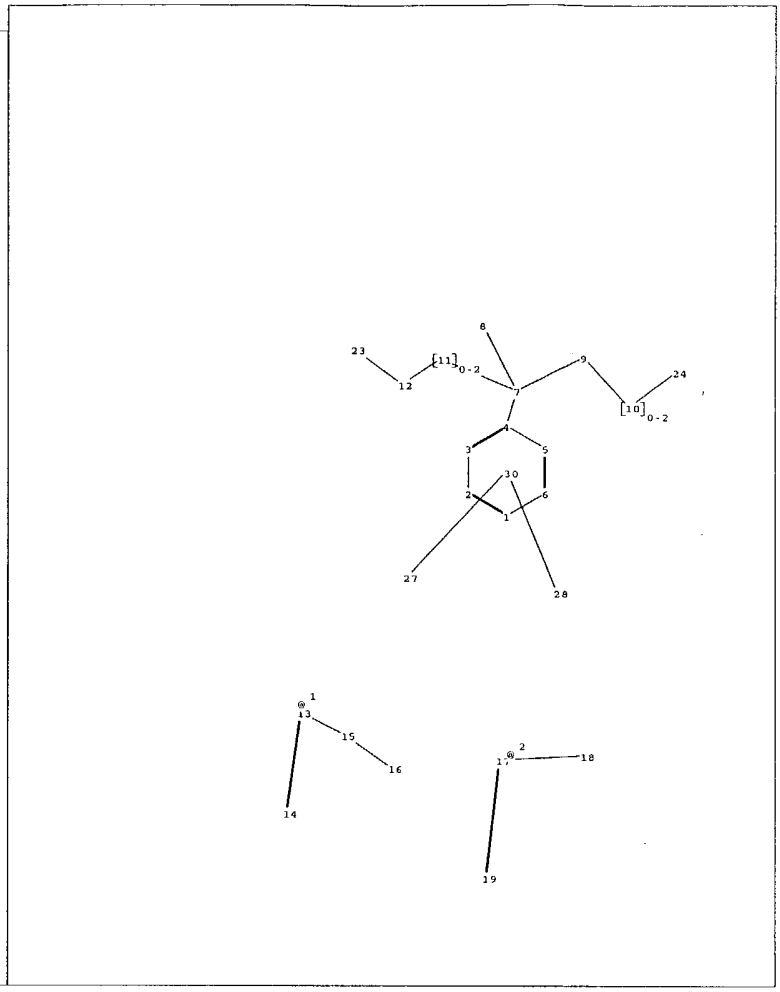
chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 19 23 24
ring nodes :
1 2 3 4 5 6
chain bonds :
4-7 7-8 7-9 7-11 9-10 10-24 11-12 12-23 13-14 13-15 15-16 17-18 17-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
10-24 12-23 13-14 13-15 15-16 17-18 17-19
exact bonds :
4-7 7-8 7-9 7-11 9-10 11-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:COOH,[*1],[*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
23:CLASS 24:CLASS

C:\stnweb\Queries\3k.str





chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 19 23 24 27 28
ring nodes :
1 2 3 4 5 6
chain bonds :
4-7 7-8 7-9 7-11 9-10 10-24 11-12 12-23 13-14 13-15 15-16 17-18 17-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
10-24 12-23 13-14 13-15 15-16 17-18 17-19
exact bonds :
4-7 7-8 7-9 7-11 9-10 11-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:COOH,[*1],[*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
23:CLASS 24:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS

```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS  4  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus
 NEWS  5  FEB 05   German (DE) application and patent publication number format
                   changes
 NEWS  6  MAR 03   MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03   FRANCEPAT now available on STN
 NEWS  9  MAR 29   Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29   WPIFV now available on STN
 NEWS 11  MAR 29   New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 12  APR 26   PROMT: New display field available
 NEWS 13  APR 26   IFIPAT/IFIUDB/IFICDB: New super search and display field
                   available
 NEWS 14  APR 26   LITALERT now available on STN
 NEWS 15  APR 27   NLDB: New search and display fields available
 NEWS 16  May 10   PROUSDDR now available on STN
 NEWS 17  May 19   PROUSDDR: One FREE connect hour, per account, in both May
                   and June 2004
 NEWS 18  May 12   EXTEND option available in structure searching
 NEWS 19  May 12   Polymer links for the POLYLINK command completed in REGISTRY

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
```

provided by InfoChem.

STRUCTURE FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9
DICTIONARY FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

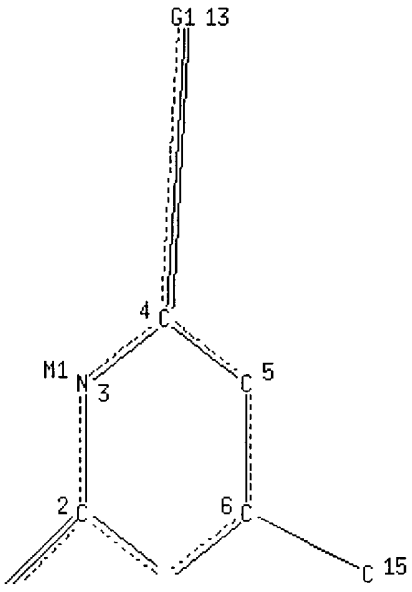
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

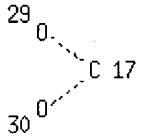
=>
L1 STRUCTURE UPLOADED

=> l1
L1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l1
L1 HAS NO ANSWERS
L1 STR
0 31 S 32

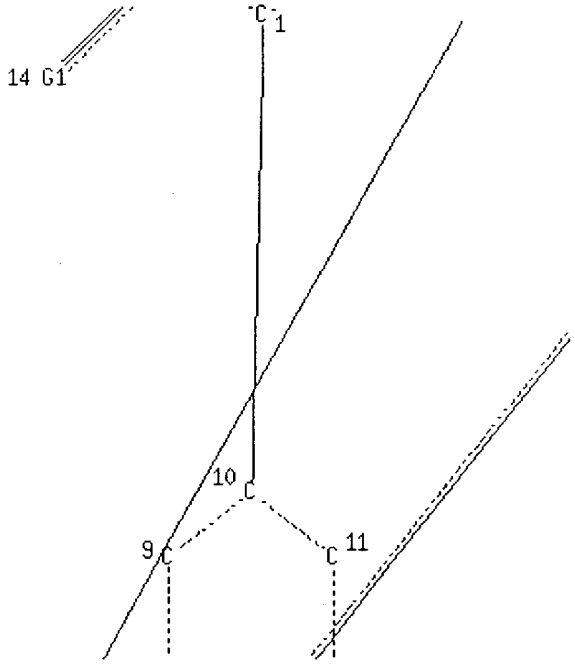


Page 1-A

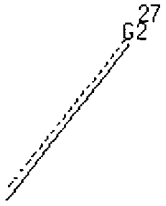


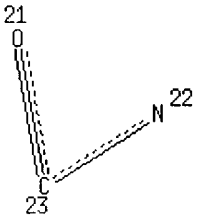
C 16

Page 1-B

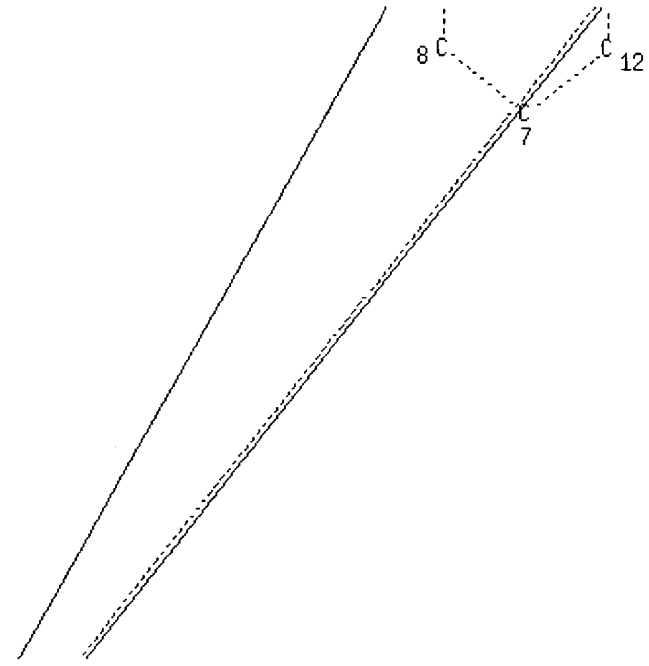


Page 2-A

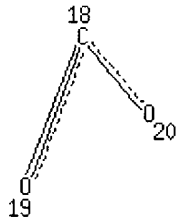




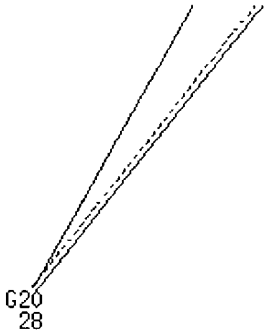
Page 2-B



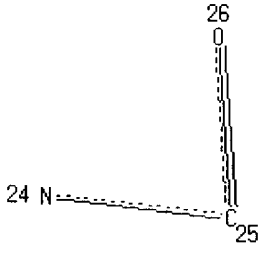
Page 3-A



Page 3-B



Page 4-A



Page 4-B
VAR G1=31/32
VAR G2=17/18/24
REP G20=(0-2) 16-15 16-27
NODE ATTRIBUTES:

```
HCOUNT  IS M1      AT   3
NSPEC   IS R       AT   1
NSPEC   IS R       AT   2
NSPEC   IS R       AT   3
NSPEC   IS R       AT   4
NSPEC   IS R       AT   5
NSPEC   IS R       AT   6
NSPEC   IS R       AT   7
NSPEC   IS R       AT   8
NSPEC   IS R       AT   9
NSPEC   IS R       AT  10
NSPEC   IS R       AT  11
NSPEC   IS R       AT  12
NSPEC   IS C       AT  13
NSPEC   IS C       AT  14
NSPEC   IS C       AT  15
NSPEC   IS C       AT  16
NSPEC   IS C       AT  17
NSPEC   IS C       AT  18
NSPEC   IS C       AT  19
NSPEC   IS C       AT  20
NSPEC   IS C       AT  21
NSPEC   IS C       AT  22
NSPEC   IS C       AT  23
NSPEC   IS C       AT  24
NSPEC   IS C       AT  25
NSPEC   IS C       AT  26
NSPEC   IS C       AT  27
NSPEC   IS C       AT  28
NSPEC   IS C       AT  29
NSPEC   IS C       AT  30
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  15 16 17 18 19 20 21 22 23 24 25 26 29 30 31 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  32

STEREO ATTRIBUTES: NONE


=> s l1
SAMPLE SEARCH INITIATED 16:44:23 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      4 TO ITERATE

100.0% PROCESSED       4 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            4 TO      200
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:44:30 FILE 'REGISTRY'
```

```
FULL SCREEN SEARCH COMPLETED -      43 TO ITERATE

100.0% PROCESSED      43 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

L3             0 SEA SSS FUL L1

=> file beilstein
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     158.36     158.57

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004
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FILE RELOADED ON OCTOBER 20, 2002
FILE LAST UPDATED ON MARCH 30,2004

FILE COVERS 1771 TO 2003.
 FILE CONTAINS  8,932,479 SUBSTANCES

>>> PLEASE NOTE: Reaction data and substance data are stored in
    separate documents and can not be searched together in one
    query.
    Reaction data for BEILSTEIN compounds may be displayed
    immediately with the display codes PRE (preparations) and REA
    (reactions). A substance answer set retrieved after the search
    for a chemical name, a molecular formula or a structure search
    for example can be restricted to compounds with available
    reaction information by concatenation with PRE/FA, REA/FA or
    more general with RX/FA. The BEILSTEIN Registry Number (BRN)
    is the link between a BEILSTEIN compound and belonging reactions.
    For more detailed reaction searches BRNs can be selected from
    substance answer sets and searched in the next step as reaction
    partner BRNs - Reactant (RX.RBRN) or Product BRN (RX.PBRN).
    After a search for reaction details substance documents
    associated with reactants or products may be retrieved by
    searching RX.PBRNs or RX.RBRNs as BRNs. <<<


>>> FOR SEARCHING PREPARATIONS SEE HELP PRE  <<<

*********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.               *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE  *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE         *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                       *
* FOR PRICE INFORMATION SEE HELP COST                               *
*********************************************************************

=>
L4       STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4               STR
```
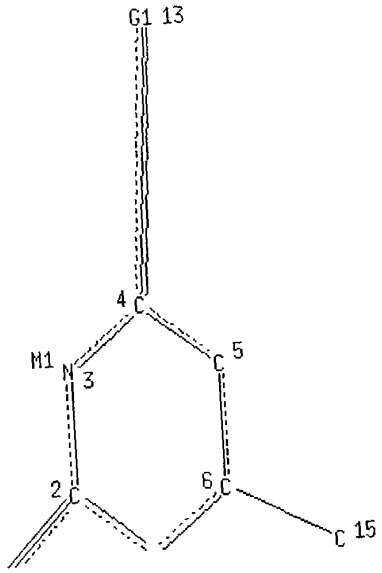
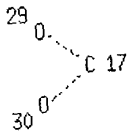
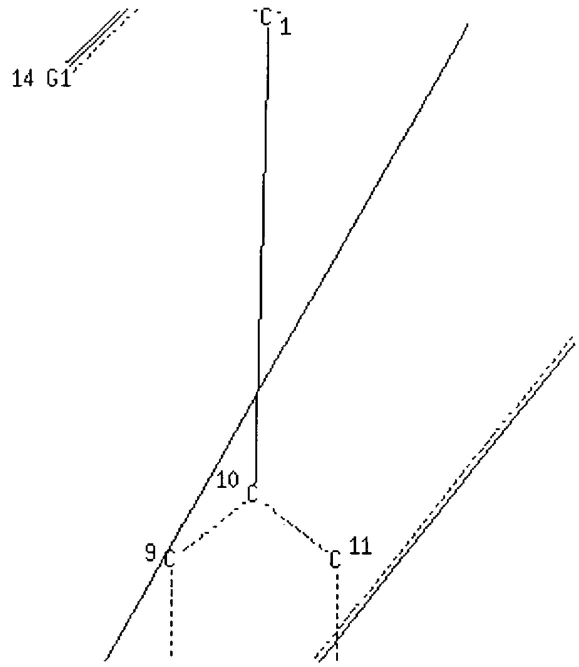

O 31 S 32



Page 1-A

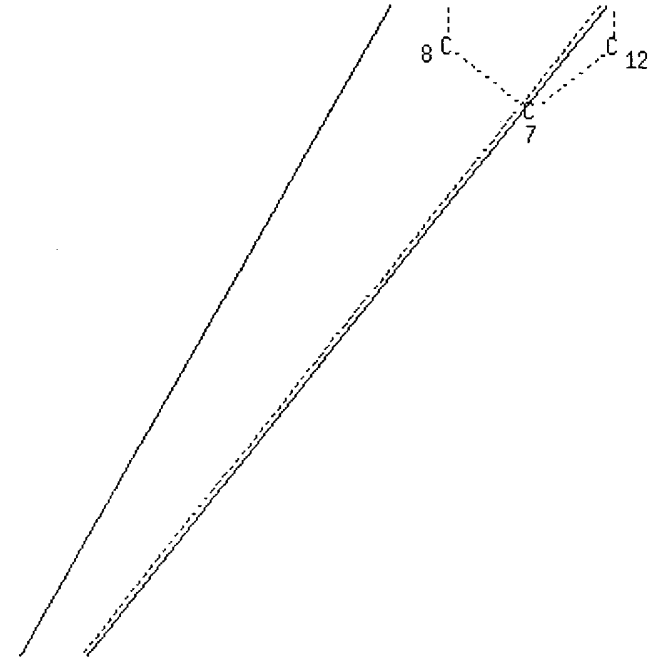


C 16
Page 1-B

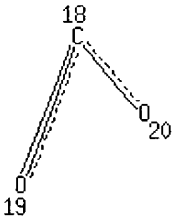


Page 2-A

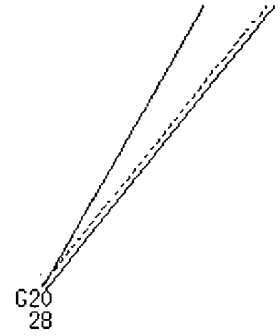
Page 2-B



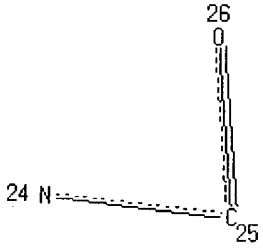
Page 3-A



Page 3-B



Page 4-A



Page 4-B
VAR G1=31/32
VAR G2=17/18/24
REP G20=(0-2) 16-15 16-27
NODE ATTRIBUTES:

```
HCOUNT  IS M1      AT   3
NSPEC   IS R       AT   1
NSPEC   IS R       AT   2
NSPEC   IS R       AT   3
NSPEC   IS R       AT   4
NSPEC   IS R       AT   5
NSPEC   IS R       AT   6
NSPEC   IS R       AT   7
NSPEC   IS R       AT   8
NSPEC   IS R       AT   9
NSPEC   IS R       AT  10
NSPEC   IS R       AT  11
NSPEC   IS R       AT  12
NSPEC   IS C       AT  13
NSPEC   IS C       AT  14
NSPEC   IS C       AT  15
NSPEC   IS C       AT  16
NSPEC   IS C       AT  17
NSPEC   IS C       AT  18
NSPEC   IS C       AT  19
NSPEC   IS C       AT  20
NSPEC   IS C       AT  21
NSPEC   IS C       AT  22
NSPEC   IS C       AT  23
NSPEC   IS C       AT  24
NSPEC   IS C       AT  25
NSPEC   IS C       AT  26
NSPEC   IS C       AT  27
NSPEC   IS C       AT  28
NSPEC   IS C       AT  29
NSPEC   IS C       AT  30
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  15 16 17 18 19 20 21 22 23 24 25 26 29 30 31 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  32

STEREO ATTRIBUTES: NONE


=> s l4
SAMPLE SEARCH INITIATED 16:45:21 FILE 'BEILSTEIN'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.04

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:             0 TO        0
PROJECTED ANSWERS:                0 TO        0

L5            0 SEA SSS SAM L4

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.12     158.69
```

```
FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
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STRUCTURE FILE UPDATES:   14 MAY 2004  HIGHEST RN 682152-60-9
DICTIONARY FILE UPDATES:  14 MAY 2004  HIGHEST RN 682152-60-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L6      STRUCTURE UPLOADED

=>  l6
L6 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l6
L6 HAS NO ANSWERS
L6                STR
 0 31 S 32
```
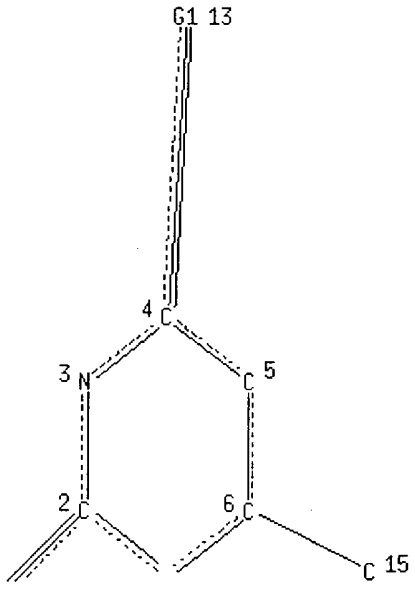
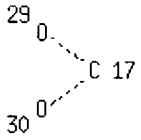
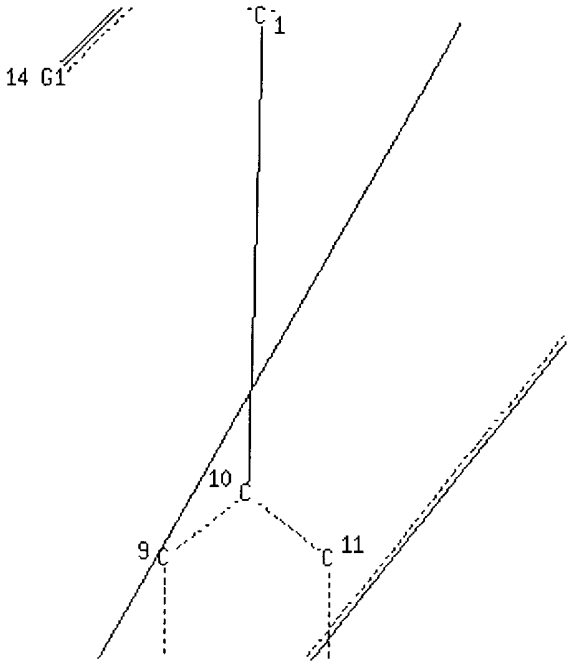



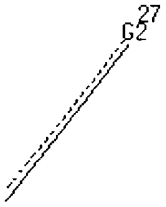
Page 1-A

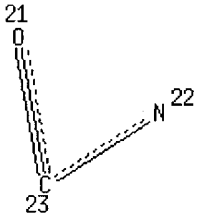


C 16
Page 1-B

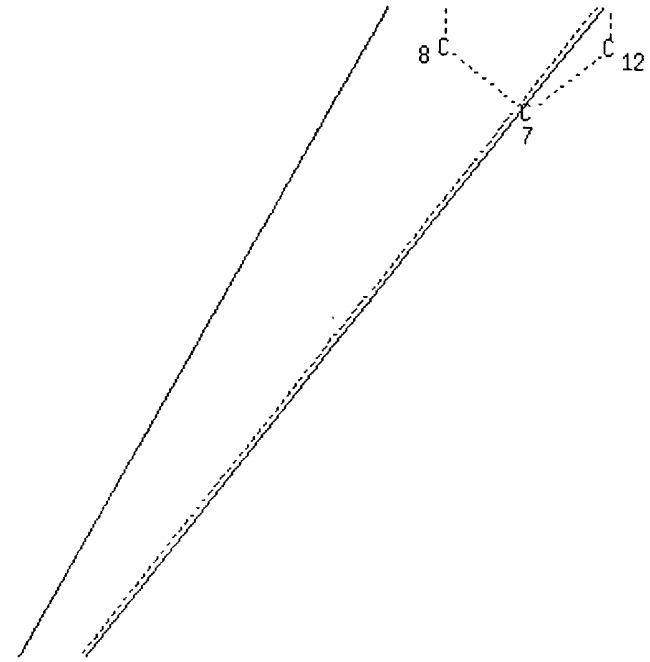


Page 2-A

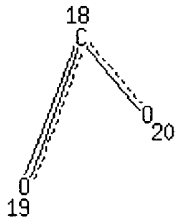




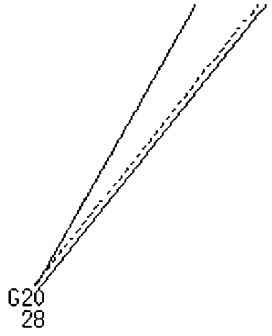
Page 2-B



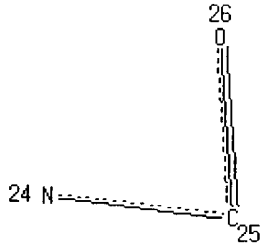
Page 3-A



Page 3-B



Page 4-A



Page 4-B
VAR G1=31/32
VAR G2=17/18/24
REP G20=(0-2) 16-15 16-27
NODE ATTRIBUTES:

```
NSPEC   IS R      AT   1
NSPEC   IS R      AT   2
NSPEC   IS R      AT   3
NSPEC   IS R      AT   4
NSPEC   IS R      AT   5
NSPEC   IS R      AT   6
NSPEC   IS R      AT   7
NSPEC   IS R      AT   8
NSPEC   IS R      AT   9
NSPEC   IS R      AT  10
NSPEC   IS R      AT  11
NSPEC   IS R      AT  12
NSPEC   IS C      AT  13
NSPEC   IS C      AT  14
NSPEC   IS C      AT  15
NSPEC   IS C      AT  16
NSPEC   IS C      AT  17
NSPEC   IS C      AT  18
NSPEC   IS C      AT  19
NSPEC   IS C      AT  20
NSPEC   IS C      AT  21
NSPEC   IS C      AT  22
NSPEC   IS C      AT  23
NSPEC   IS C      AT  24
NSPEC   IS C      AT  25
NSPEC   IS C      AT  26
NSPEC   IS C      AT  27
NSPEC   IS C      AT  28
NSPEC   IS C      AT  29
NSPEC   IS C      AT  30
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  15 16 17 18 19 20 21 22 23 24 25 26 29 30 31 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  32

STEREO ATTRIBUTES: NONE


=> s l6
SAMPLE SEARCH INITIATED 16:46:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      4 TO ITERATE

100.0% PROCESSED       4 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            4 TO      200
PROJECTED ANSWERS:               0 TO        0

L7            0 SEA SSS SAM L6

=> s l6 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:46:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     43 TO ITERATE
```

```
100.0% PROCESSED      43 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L8             0 SEA SSS FUL L6

=>
L9      STRUCTURE UPLOADED

=>  l9
L9 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l9
SAMPLE SEARCH INITIATED 16:50:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     56 TO ITERATE

100.0% PROCESSED      56 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          672 TO     1568
PROJECTED ANSWERS:               3 TO      163

L10            3 SEA SSS SAM L9

=> s l9 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:50:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   1412 TO ITERATE

100.0% PROCESSED    1412 ITERATIONS                               48 ANSWERS
SEARCH TIME: 00.00.01

L11           48 SEA SSS FUL L9

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                             313.36     472.05

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004
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FILE COVERS 1907 - 16 May 2004  VOL 140 ISS 21
FILE LAST UPDATED: 14 May 2004  (20040514/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l11
L12         69 L11

=> s l12 and castro, b?/au
           342 CASTRO, B?/AU
L13          1 L12 AND CASTRO, B?/AU

=> d l13, ibib abs fhitstr, 1

L13  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:         2000:441776  HCAPLUS
DOCUMENT NUMBER:          133:73938
TITLE:                    Preparation of 3-(3,4-dihalophenyl)-2,6-
                          dioxopiperidine-3-propionic acid alkyl esters as
                          intermediates
INVENTOR(S):              Castro, Bertrand; Dormoy, Jean-Robert; Rabion, Alain
PATENT ASSIGNEE(S):       Sanofi-Synthelabo, Fr.
SOURCE:                   PCT Int. Appl., 34 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ----------------  ----  --------       ---------------  --------
     WO 2000037445      A1   20000629       WO 1999-FR2970   19991201
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     FR 2787448         A1   20000623       FR 1998-16087    19981218
     FR 2787448         B3   20010112
     EP 1140842         A1   20011010       EP 1999-973487   19991201
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002533327      T2   20021008       JP 2000-589517   19991201
     US 6469173         B1   20021022       US 2001-857882   20010612
     US 2003032810      A1   20030213       US 2002-175126   20020619
     US 6686182         B2   20040203
PRIORITY APPLN. INFO.:                     FR 1998-16087    A  19981218
                                           WO 1999-FR2970   W  19991201
                                           US 2001-857882   A3 20010612
OTHER SOURCE(S):          CASREACT 133:73938; MARPAT 133:73938
AB   Title compds. and optically pure isomers were obtained either by
```

enantioselective enzymic hydrolysis of the racemic ester or by cyclisation of optically pure HO2CCH2CH2CR(CN)CH2CH2CO2R1 (R = 3,4-dihalophenyl, R1 = alkyl).

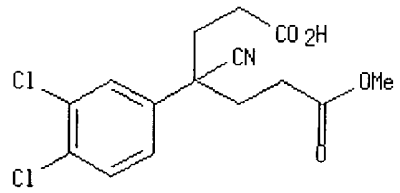
IT **279215-35-9P**

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 3-(3,4-dihalophenyl)-2,6-dioxopiperidine-3-propionic acid alkyl esters as intermediates)

RN 279215-35-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, monomethyl ester, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his

     (FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           0 S L1 FULL

     FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004
L4             STRUCTURE UPLOADED
L5           0 S L4

     FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
L6             STRUCTURE UPLOADED
L7           0 S L6
L8           0 S L6 FULL
L9             STRUCTURE UPLOADED
L10          3 S L9
L11         48 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004
L12         69 S L11
L13          1 S L12 AND CASTRO, B?/AU

=> s l12 not l13
L14         68 L12 NOT L13

=> s l14 and dormoy, j?/au
            47 DORMOY, J?/AU
L15          0 L14 AND DORMOY, J?/AU

=> s l14 and rabion, a?/au
            27 RABION, A?/AU
L16          0 L14 AND RABION, A?/AU
```

```
=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                         9.48     481.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                          ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -0.69      -0.69

FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   14 MAY 2004  HIGHEST RN 682152-60-9
DICTIONARY FILE UPDATES:  14 MAY 2004  HIGHEST RN 682152-60-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d his

     (FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           0 S L1 FULL

     FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004
L4             STRUCTURE UPLOADED
L5           0 S L4

     FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
L6             STRUCTURE UPLOADED
L7           0 S L6
L8           0 S L6 FULL
L9             STRUCTURE UPLOADED
L10          3 S L9
L11         48 S L9 FULL

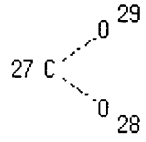
     FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004
L12         69 S L11
L13          1 S L12 AND CASTRO, B?/AU
L14         68 S L12 NOT L13
L15          0 S L14 AND DORMOY, J?/AU
L16          0 S L14 AND RABION, A?/AU
```

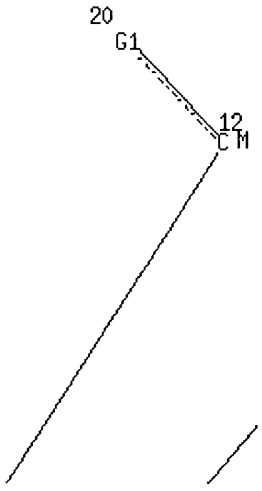
FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004

=> s l11/prep
'PREP' IS NOT A VALID CROSSOVER QUALIFIER FOR L11
Answer sets created in a different file may be field qualified with a limited set of qualifiers. Enter HELP CROSSOVER at an arrow prompt (=>) for specific information.

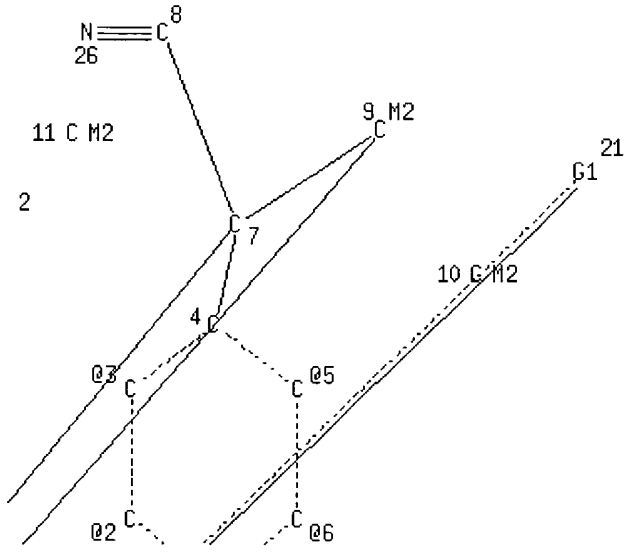
=>
L17 STRUCTURE UPLOADED

=> d l17
L17 HAS NO ANSWERS
L17 STR

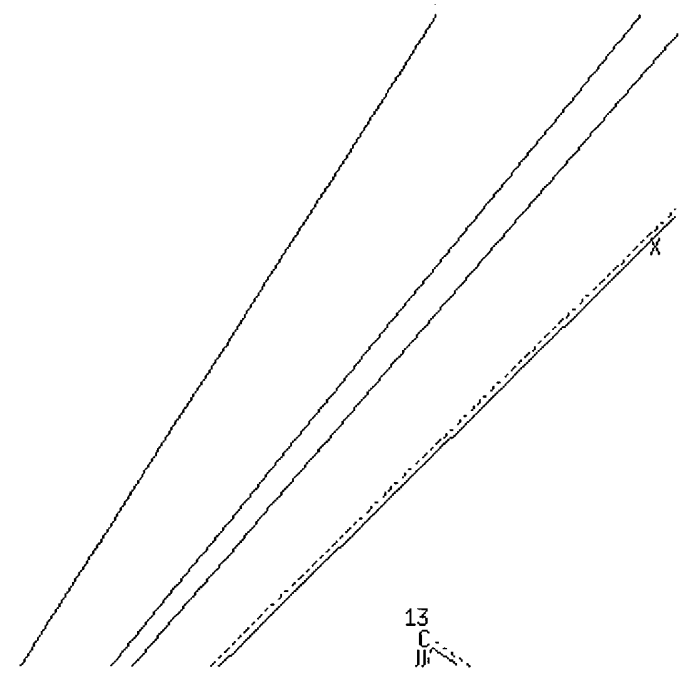




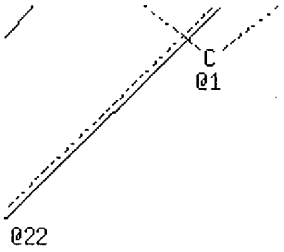
Page 1-A



Page 1-B

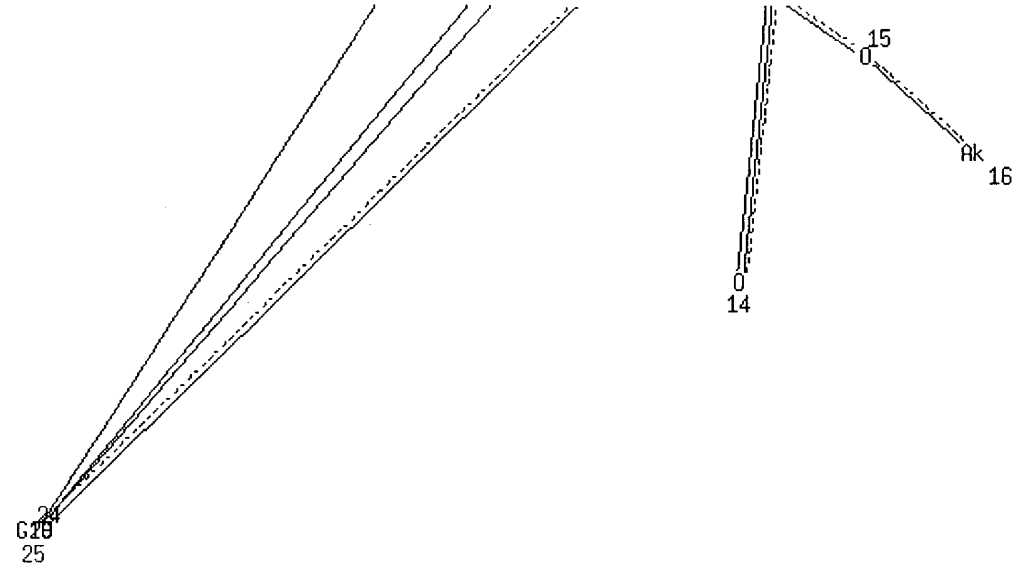


Page 2-A

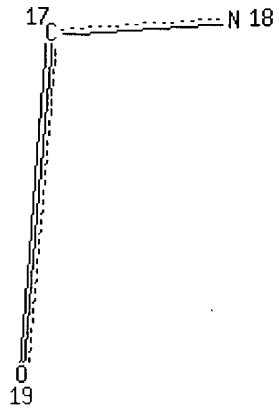


X @23

Page 2-B



Page 3-A

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Page 3-B
VAR G1=27/13/17
REP G19=(0-2) 11-7 11-12
REP G20=(0-2) 10-9 10-21
VPA 22-1/2/3/5/6 S
VPA 23-1/2/3/5/6 S
NODE ATTRIBUTES:
HCOUNT  IS M2     AT   9
HCOUNT  IS M2     AT  10
HCOUNT  IS M2     AT  11
HCOUNT  IS M2     AT  12
NSPEC   IS R      AT   1
NSPEC   IS R      AT   2
NSPEC   IS R      AT   3
NSPEC   IS R      AT   4
NSPEC   IS R      AT   5
NSPEC   IS R      AT   6
NSPEC   IS C      AT   7
NSPEC   IS C      AT   8
NSPEC   IS C      AT   9
NSPEC   IS C      AT  10
NSPEC   IS C      AT  11
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NSPEC   IS C      AT  19
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NSPEC   IS C      AT  22
NSPEC   IS C      AT  23
NSPEC   IS C      AT  24
NSPEC   IS C      AT  25
NSPEC   IS C      AT  26
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   7  8  9 10 11 12 13 14 15 16 17 18 19 22 23 26 27
          28 29
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  29
```

```
STEREO ATTRIBUTES: NONE


=> s l17
SAMPLE SEARCH INITIATED 16:54:34 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     164 TO ITERATE

100.0% PROCESSED     164 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         2512 TO     4048
PROJECTED ANSWERS:               0 TO        0

L18            0 SEA SSS SAM L17

=> s l17 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:54:38 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    3193 TO ITERATE

100.0% PROCESSED    3193 ITERATIONS                                9 ANSWERS
SEARCH TIME: 00.00.01

L19            9 SEA SSS FUL L17

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   157.10     638.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -0.69

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FILE COVERS 1907 - 16 May 2004  VOL 140 ISS 21
FILE LAST UPDATED: 14 May 2004  (20040514/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
```

```
=> s l19
L20         26 L19

=> s l19/prep
            26 L19
       3147996 PREP/RL
L21         26 L19/PREP
                 (L19 (L) PREP/RL)

=> s l20 and castro, b?/au
           342 CASTRO, B?/AU
L22          1 L20 AND CASTRO, B?/AU

=> d his

     (FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004
L1              STRUCTURE UPLOADED
L2            0 S L1
L3            0 S L1 FULL

     FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004
L4              STRUCTURE UPLOADED
L5            0 S L4

     FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
L6              STRUCTURE UPLOADED
L7            0 S L6
L8            0 S L6 FULL
L9              STRUCTURE UPLOADED
L10           3 S L9
L11          48 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004
L12          69 S L11
L13           1 S L12 AND CASTRO, B?/AU
L14          68 S L12 NOT L13
L15           0 S L14 AND DORMOY, J?/AU
L16           0 S L14 AND RABION, A?/AU

     FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004
L17             STRUCTURE UPLOADED
L18           0 S L17
L19           9 S L17 FULL

     FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004
L20          26 S L19
L21          26 S L19/PREP
L22           1 S L20 AND CASTRO, B?/AU

=> s l22 not l13
L23          0 L22 NOT L13

=> d l22, ibib abs fhitstr, 1

L22  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
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ACCESSION NUMBER:         2000:441776  HCAPLUS
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DOCUMENT NUMBER: 133:73938
TITLE: Preparation of 3-(3,4-dihalophenyl)-2,6-dioxopiperidine-3-propionic acid alkyl esters as intermediates
INVENTOR(S): **Castro, Bertrand**; Dormoy, Jean-Robert; Rabion, Alain
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037445	A1	20000629	WO 1999-FR2970	19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2787448	A1	20000623	FR 1998-16087	19981218
FR 2787448	B3	20010112		
EP 1140842	A1	20011010	EP 1999-973487	19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533327	T2	20021008	JP 2000-589517	19991201
US 6469173	B1	20021022	US 2001-857882	20010612
US 2003032810	A1	20030213	US 2002-175126	20020619
US 6686182	B2	20040203		

PRIORITY APPLN. INFO.:

FR 1998-16087	A	19981218
WO 1999-FR2970	W	19991201
US 2001-857882	A3	20010612

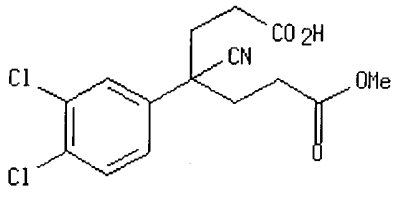
OTHER SOURCE(S): CASREACT 133:73938; MARPAT 133:73938

AB Title compds. and optically pure isomers were obtained either by enantioselective enzymic hydrolysis of the racemic ester or by cyclisation of optically pure HO2CCH2CH2CR(CN)CH2CH2CO2R1 (R = 3,4-dihalophenyl, R1 = alkyl).

IT **279215-35-9P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 3-(3,4-dihalophenyl)-2,6-dioxopiperidine-3-propionic acid alkyl esters as intermediates)

RN 279215-35-9 HCAPLUS
CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, monomethyl ester, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



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REFERENCE COUNT:          4      THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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     FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004
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L2           0 S L1
L3           0 S L1 FULL

     FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004
L4             STRUCTURE UPLOADED
L5           0 S L4

     FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
L6             STRUCTURE UPLOADED
L7           0 S L6
L8           0 S L6 FULL
L9             STRUCTURE UPLOADED
L10          3 S L9
L11         48 S L9 FULL

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L12         69 S L11
L13          1 S L12 AND CASTRO, B?/AU
L14         68 S L12 NOT L13
L15          0 S L14 AND DORMOY, J?/AU
L16          0 S L14 AND RABION, A?/AU

     FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004
L17            STRUCTURE UPLOADED
L18          0 S L17
L19          9 S L17 FULL

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L20         26 S L19
L21         26 S L19/PREP
L22          1 S L20 AND CASTRO, B?/AU
L23          0 S L22 NOT L13

=> s l21 not l22
L24         25 L21 NOT L22

=> d l24, ibib abs fhitstr, 1-25

L24  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2004 ACS on STN
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ACCESSION NUMBER:         2001:896499  HCAPLUS
DOCUMENT NUMBER:          136:20072
TITLE:                    1-Benzoyl-3-[2-[4-(1H-benzimidazole-2-
                          carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine
                          derivatives and analogs as histamine and tachykinin
                          receptor antagonists useful for the treatment of
                          allergic diseases
INVENTOR(S):              Burkholder, Timothy P.; Bratton, Larry D.; Kudlacz,
                          Elizabeth M.; Maynard, George P.; Kane, John M.;
```
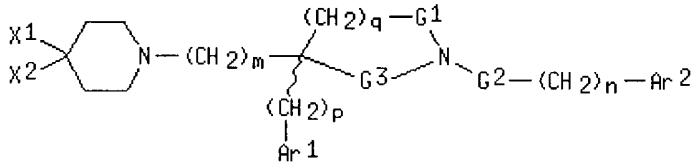

Santiago, Braulio
PATENT ASSIGNEE(S): Aventis Pharmaceuticals, Inc., USA
SOURCE: U.S., 77 pp., Cont.-in-part of U.S. Ser. No. 501,914, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6329392	B1	20011211	US 1998-79924	19980515
CA 2198084	AA	19960229	CA 1995-2198084	19950817
CN 1158612	A	19970903	CN 1995-195283	19950817
CN 1067385	B	20010620		
HU 76644	A2	19971028	HU 1997-1257	19950817
HU 221434	B	20021028		
AT 177095	E	19990315	AT 1995-931551	19950817
ES 2132709	T3	19990816	ES 1995-931551	19950817
ZA 9507033	A	19960416	ZA 1995-7033	19950822
IL 115040	A1	20000229	IL 1995-115040	19950823
TW 430663	B	20010421	TW 1995-84108797	19950823

PRIORITY APPLN. INFO.: US 1994-295960 B2 19940825
US 1995-501914 B2 19950713
OTHER SOURCE(S): MARPAT 136:20072
GI



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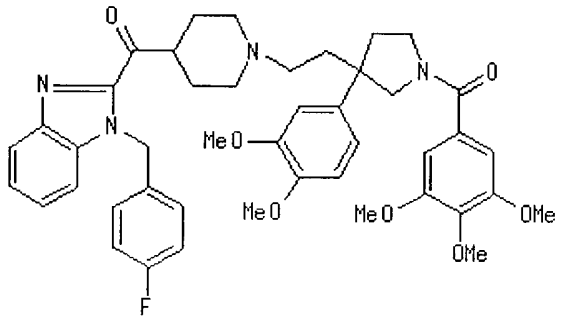


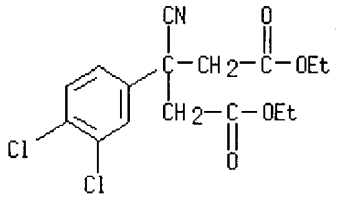
II

AB The present invention relates to novel substituted piperidine derivs. I wherein: G1 is CH2 or CO; G2 is CH2 or CO; G3 is CH2 or CO; m is 2 or 3; n is 0 or 1; q is 1 or 2; p is 0 or 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, pyridyl; X1 and X2 are defined in one of (A), (B), or (C): (A) X1 = H and X2 = substituted benzothiazole-2-carbonyl, diphenylmethyl, benzimidazolyl-2-carbonyl; (B) X1 = OH and X2 = substituted benzothiazol-2-yl, benzimidazol-2-yl; (C) X2 = (R5C6H4)C(Z1)(C6H4R6) wherein R5, R6 = from 1 to 3 substituents chosen independently from, e.g., H, halo, CF3, and X1 and Z1 taken together form a second bond between the carbon atoms bearing X1 and Z1; provided than

when G1 is CO, then G2 and G3 are CH2, and that when G2 is CO, then G1 and G3 are CH2, and that when G3 is CO, then G1 and G2 are CH2; stereoisomers thereof, and pharmaceutically acceptable salts thereof which are useful as histamine receptor antagonists and tachykinin receptor antagonists. Such antagonists are useful in the treatment of allergic diseases including: seasonal rhinitis, allergic rhinitis, and sinusitis. Thus, e.g., substitution reaction of 4-[1-(4-fluorobenzyl)-1H-benzimidazole-2-carbonyl]piperidine with 1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine (prepn. given) afforded II which exhibited H1 receptor antagonism in vitro with pA2 = 7.50, and NK1 receptor binding affinity with IC50 = 31 nM.

IT **40878-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(1-benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivs. and analogs as histamine and tachykinin receptor antagonists useful for treatment of allergic diseases)

RN 40878-10-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:781460 HCAPLUS
DOCUMENT NUMBER: 135:344508
TITLE: Preparation of substituted benzimidazolyl[1,4]diazepanes useful as histamine and tachykinin receptor antagonists
INVENTOR(S): Maynard, George D.; Le, Tieu-binh
PATENT ASSIGNEE(S): George, Maynard,, USA
SOURCE: U.S. Pat. Appl. Publ., 122 pp., Cont.-in-part of U.S. 6,194,406.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001034343	A1	20011025	US 2000-739741	20001218
US 6423704	B2	20020723		
US 6194406	B1	20010227	US 1997-513847	19971029

PRIORITY APPLN. INFO.: US 1995-70907P P 19951220
US 1996-736411 B2 19961024
US 1997-513847 A2 19971029

OTHER SOURCE(S): MARPAT 135:344508
GI

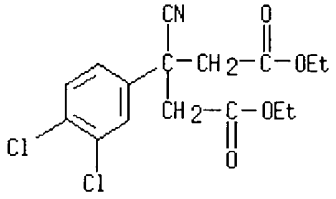
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [m = 1 - 2; p = 0 - 1; G = CO, COCH2, SO2; R30 = alkyl, vinyl, alkyl-oxy-alkyl-cyclopropyl, alkylheterocyclyl; R33 = H, alkoxy, heterocyclyl, sulfonyloxy, etc.; R31-32 = H, alkoxy] were prepd. Over 100 synthetic examples were provided. E.g., 3,4-dimethoxyacetonitrile was alkylated twice with Et bromoacetate (THF, NaHMDS, dry-ice/acetone bath) and converted to 5-oxopyrrolidin-3-yl deriv. II (CoCl2•6H2O, MeOH, 20°C). II was converted to the pyrrolidine-alc. (THF, LAH, reflux, 18 h), N-acylated (CH2Cl2, NMM, 5°C, 3,4,5-(MeO)3C6H2COCl), converted to the mesylate (CH2Cl2, MsCl, Et3N, < 2°C - room temp. 18 h) and coupled to 4-(1-(2-ethoxyethyl)-1H-benzimidazol-2-yl)[1,4]diazepane (prepn. given, i-Pr2NEt, CH3CN, NaI, reflux, 3 days) to give example compd. III. I are histamine and tachykinin receptor antagonists (no data). Such antagonists are useful in the treatment of allergic rhinitis, inflammatory bowel diseases, Crohn's disease, ulcerative colitis, etc.

IT **40878-10-2P**, 3-Cyano-3-(3,4-dichlorophenyl)pentanedioic acid diethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of substituted benzimidazolyl[1,4]diazepanes useful as histamine and tachykinin receptor antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

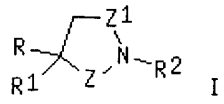
Full Text | Citing References

ACCESSION NUMBER: 2001:240149 HCAPLUS
DOCUMENT NUMBER: 134:266309
TITLE: Preparation of 4-(2-benzimidazolylamino)piperidines as histamine and tachykinin receptor antagonists
INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: U.S., 106 pp., Cont.-in-part of U.S. Ser. No. 734,508, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6211199	B1	20010403	US 1997-513846		19971215
PRIORITY APPLN. INFO.:			US 1995-34609P	P	19951117
			US 1996-734508	B2	19961017

OTHER SOURCE(S): MARPAT 134:266309
GI

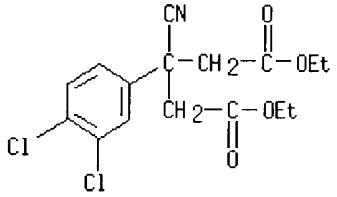


I

AB Title compds., e.g., I [R = R4Z4(CH2)m; R1 = (un)substituted Ph, -pyridinyl, -thienyl, etc.; R2 = (un)substituted (alkylenedioxy) benzyl, -benzoyl, etc.; R4 = e.g., (un)substituted 2-benzimidazolylamino; Z,Z1 = CH2 or CO; Z4 = piperidine-4,1-diyl; m = 2 or 3] were prepd. as histamine and tachykinin receptor antagonists (no data). Thus, 4-[1-(2-furylmethyl)-2-benzimidazolylamino]piperidine was condensed with 2-[1-[2-methoxy-5-(1-tetrazolyl)benzoyl]-3-phenyl-3-pyrrolidinyl]ethyl methanesulfonate (prepn each given) to give I [R = R4Z4CH2CH2, R1 = Ph, R2 = 2-methoxy-5-(1-tetrazolyl)benzoyl, R4 = 1-(2-furylmethyl)-2-benzimidazolylamino, Z = Z1 = CH2, Z4 = piperidine-4,1-diyl].

IT **40878-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of (benzimidazolylamino)piperidines as antiallergics)

RN 40878-10-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

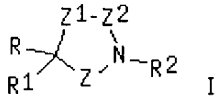
ACCESSION NUMBER:	2001:149048 HCAPLUS
DOCUMENT NUMBER:	134:193454
TITLE:	Preparation of N-(2-benzimidazolyl)-1,4-diazepanes as histamine and tachykinin receptor antagonists
INVENTOR(S):	Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Kudlacz, Elizabeth M.; Santiago, Braulio
PATENT ASSIGNEE(S):	Aventis Pharmaceuticals Inc., USA
SOURCE:	U.S., 108 pp., Cont.-in-part of U.S. Ser. No. 736,411. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6194406	B1	20010227	US 1997-513847	19971029
US 2001034343	A1	20011025	US 2000-739741	20001218
US 6423704	B2	20020723		

PRIORITY APPLN. INFO.: US 1995-70907P P 19951220
US 1996-736411 B2 19961024
US 1997-513847 A2 19971029

OTHER SOURCE(S): MARPAT 134:193454

GI



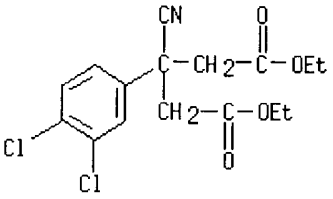
I

AB Title compds. [I; R = R5Z5Z4(CH2)m; R1 = (CH2)rR4; R2 = Z3(CH2)nR3; R3 = (un)substituted Ph, -1,3-benzodioxol-5-yl, -1,4-benodioxan-6-yl; R4 = (un)substituted Ph, -naphthyl, pyridinyl, -thienyl; R5 = H, (oxa)alkyl, (hetero)arylalkyl, etc.; Z,Z2 = CH2 or CO; Z1 = CH2 or CH2CH2; Z3 = CH2, CHMe, CO; Z4 = 1,4-diazepan-1,4-diyl; Z5 = (un)substituted benzimidazole-1,2-diyl; m = 2 or 3; n,r = 0 or 1] were prepd. as histamine and tachykinin receptor antagonists (no data). Thus, e.g., I [R = 2-[4-[1-(2-ethoxyethyl)benzimidazol-2-yl][1,4]diazepan-1-yl]ethyl, R1 = 3,4-(MeO)2C6H3, R2 = COC6H2(OMe)3-3,4,5, Z = Z1 = Z2 = CH2] was prepd.

IT **40878-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of benzimidazolyldiazepanes as antiallergics and antiinflammatories)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

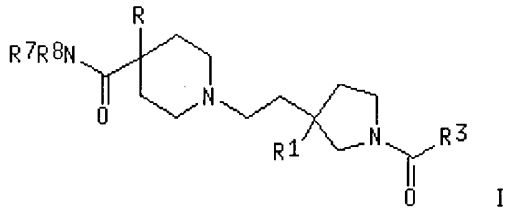
Full Text | Citing References

ACCESSION NUMBER: 1999:56370 HCAPLUS
DOCUMENT NUMBER: 130:124994
TITLE: Preparation of 4-aryl-1-[2-(1-benzoyl-3-pyrrolidinyl)ethyl]piperidine-4-carboxamides as NK1 and NK2 receptor antagonists
INVENTOR(S): Burkholder, Timothy P.; Maynard, George D.; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: U.S., 30 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5861417	A	19990119	US 1997-990672	19971215

PRIORITY APPLN. INFO.: US 1997-990672 19971215
OTHER SOURCE(S): MARPAT 130:124994
GI

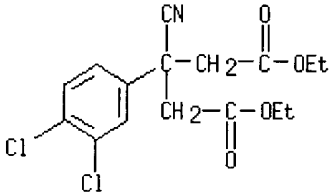


I

AB Title compds. [I; R = (un)substituted Ph or -pyridyl; R1 = (un)substituted Ph; R2 = ZR3; R3 = 1- or 5-tetrazolyl, 1,2,4-triazol-4-yl, etc.; R7,R8 = H; NR7R8 = piperidino, morpholino, (4-methyl)piperazino, pyrrolidino; Z = 6-(un)substituted-1,3-phenylene] were prepd. Thus, (S)-1-tert-butoxycarbonyl-3-(3,4-dichlorophenyl)-3-(2-mesyloxyethyl)pyrrolidine was aminated by 4-phenylpiperidine-4-carboxamide (prepn. each given) and the deprotected product amidated by 2-methoxy-5-(1-tetrazolyl)benzoic acid (prepn. given) to give (R)-I [R = Ph, R1 = C6H3Cl2-3,4, R2 = 2-methoxy-5-(1-tetrazolyl)phenyl, R7 = R8 = H]. Data for biol. activity of I were given.

IT **40878-10-2P**, 3-Cyano-3-(3,4-dichlorophenyl)-pentanedioic acid diethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of 4-aryl-1-[2-(1-benzoyl-3-pyrrolidinyl)ethyl]piperidine-4-carboxamides as NK1 and NK2 receptor antagonists)

RN 40878-10-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

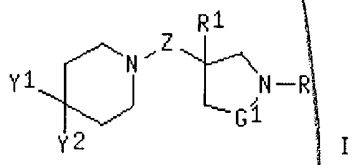
ACCESSION NUMBER: 1998:689192 HCAPLUS
DOCUMENT NUMBER: 129:330656
TITLE: Preparation of 1-(3-pyrrolidinylalkyl)-4-piperidinecarboxamides as tachykinin antagonists
INVENTOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Le

Tieu-bihn; Maynard, George D.
PATENT ASSIGNEE(S): Hoechst Marion Roussel Inc., USA
SOURCE: U.S., 93 pp., Cont.-in-part of U.S. 5,635,510.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5824690	A	19981020	US 1997-798664	19970211
ZA 9403091	A	19950112	ZA 1994-3091	19940504
US 5635510	A	19970603	US 1994-332027	19941031

PRIORITY APPLN. INFO.:
US 1993-58606 B2 19930506
US 1994-225371 B2 19940419
US 1994-332027 A2 19941031

OTHER SOURCE(S): MARPAT 129:330656
GI

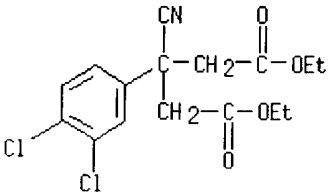


I

AB Title compds. [I; R = G2(CH2)nR2; G1,G2 = CH2 or CO; R1 = (un)substituted Ph, -naphthyl, pyridyl, etc.; R2 = (un)substituted Ph or -pyridyl; Y1 = CONHR5 or CONR6R7; R5 = H, alkyl, (CH2)qNR6R7, etc.; R6,R7 = alkyl; NR6R7 = heterocyclyl; Y2 = (un)substituted phenyl(methyl), -pyridyl, -thienyl; Y1Y2 = atoms to complete a ring; Z = (CH2)2-3; n = 0 or 1; q = 2 or 3] were prepd. Thus, 3,4-Cl2C6H3CH2CN was biscondensed with BrCH2CO2Et and the reduced product cyclized to give, after redn. and N-benzoylation, 1-benzoyl-3-(2-hydroxyethyl)-3-(3,4-dichlorophenyl)pyrrolidine. The latter was treated with MeSO2Cl and the product aminated by 4-phenylpiperidine-4-carboxamide (prepn. given) to give I (G1 = CH2, R = Bz, R1 = C6H3Cl2-3,4, Y1 = CONH2, Y2 = Ph, Z = CH2CH2). Data for biol. activity of I were given.

IT **40878-10-2P**, Diethyl 3-cyano-3-(3,4-dichlorophenyl))pentanedioate
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of 1-(3-pyrrolidinylalkyl)-4-piperidinecarboxamides as tachykinin antagonists)

RN 40878-10-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

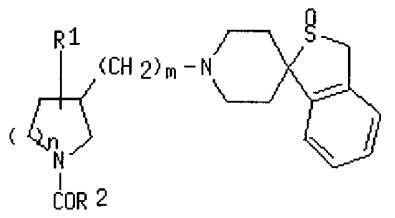
L24 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:665875 HCAPLUS
DOCUMENT NUMBER: 129:343481
TITLE: Preparation of N-(pyrrolidinylalkyl)spiro[benzo[c]thiophene-1(3H),4'-piperidine] S-oxide derivatives as substance P and neurokinin A receptor antagonists
INVENTOR(S): Nishi, Takehide; Fukazawa, Tetsuya; Yamaguchi, Takeshi; Ito, kazuhiro; Ishibashi, Kimisige; Tamura, Masakazu
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10273489	A2	19981013	JP 1998-13860	19980127
PRIORITY APPLN. INFO.:			JP 1997-18079	19970131

OTHER SOURCE(S): MARPAT 129:343481
GI



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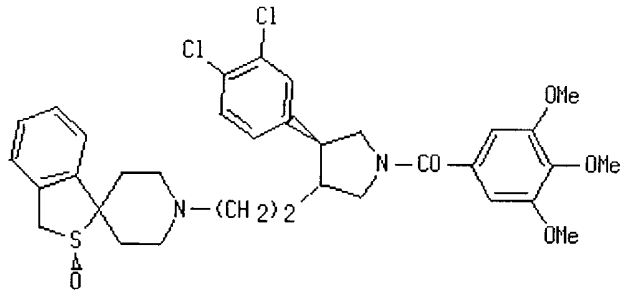


II

AB The title compds. [I; R1 = halophenyl; R2 = lower (halo)alkyl- or (halo)alkoxyphenyl; m, n = 1-3] are prepd. and specific compds. I are claimed. Also claimed are (1) antagonists of neurokinin 1 (NK1) and neurokinin 2 (NK2) receptor, (2) preventives or remedies for diseases mediated by tachykinin, and (3) preventives or remedies for asthma, bronchitis, rhinitis, allergy, and pollakiuria, contg. the compds. I as the reactive ingredients. Thus, spiro[benzo[c]thiophen-1(3H),4'-piperidin]-(2S)-oxide hydrochloride (prepn. given), 2-[(3S)-(3,4-dichlorophenyl)-1-(3,4,5-trimethoxybenzoyl)pyrrolidin-3-yl]ethyl methanesulfonate (prepn. given), NaHCO3, and KI were suspended in DMF and heated with stirring at 80° for 8 h to give the title compd. (II). II in vitro showed IC50 of 5.1 ng/mL for inhibiting the binding of

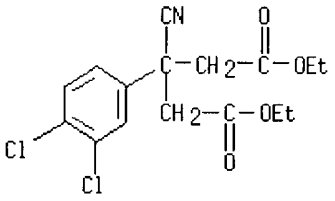
[3H]substance P to NK1 receptor prepn. from Hartley guinea pig's lung air way and IC50 of 5.8 ng/mL for inhibiting the binding of [3H]-SR-48968 to NK2 receptor prepn. from Hartley guinea pig's ileum. A tablet and a capsule formulation contg. II were described.

IT **40878-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of N-(pyrrolidinylalkyl)spiro[benzo[c]thiophene-piperidine] S-oxide derivs. as substance P and neurokinin A receptor antagonists for drugs)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:424245 HCAPLUS
DOCUMENT NUMBER: 129:95498
TITLE: Novel heterocyclic carboxy-substituted cyclic carboxamide derivatives useful as tachykinin receptor antagonists
INVENTOR(S): Burkholder, Timothy P.; Maynard, George D.; Kudlacz, Elisabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9827085	A1	19980625	WO 1997-US21586	19971121
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5977139	A	19991102	US 1997-971891	19971117
AU 9853627	A1	19980715	AU 1998-53627	19971121
AU 718984	B2	20000504		
EP 946545	A1	19991006	EP 1997-950690	19971121
EP 946545	B1	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1240443	A	20000105	CN 1997-180774	19971121

CN 1098259	B	20030108			
BR 9714156	A	20000208	BR 1997-14156	19971121	
NZ 335883	A	20010727	NZ 1997-335883	19971121	
AT 205200	E	20010915	AT 1997-950690	19971121	
ES 2162686	T3	20020101	ES 1997-950690	19971121	
PT 946545	T	20020228	PT 1997-950690	19971121	
JP 2002512596	T2	20020423	JP 1998-527720	19971121	
RU 2199535	C2	20030227	RU 1999-115883	19971121	
CA 2275602	C	20030722	CA 1997-2275602	19971121	
EE 4117	B1	20030815	EE 1999-254	19971121	
ZA 9711264	A	19980623	ZA 1997-11264	19971215	
NO 9903012	A	19990818	NO 1999-3012	19990618	
KR 2000057667	A	20000925	KR 1999-705495	19990618	
HK 1020571	A1	20020517	HK 1999-105551	19991130	

PRIORITY APPLN. INFO.:

US 1996-794157	A	19961219
US 1997-971891	A	19971117
WO 1997-US21586	W	19971121

OTHER SOURCE(S): MARPAT 129:95498

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

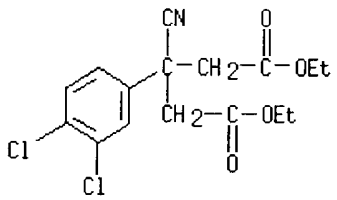
AB The invention relates to novel carboxy-substituted cyclic carboxamide derivs. I and stereoisomers and pharmaceutically acceptable salts thereof [wherein either G1 or G2 = CH2, while other = CO; m = 2 or 3; n = 0 or 1; R1 = 1-3 of H, halo, CF3, alkyl, alkoxy; R2 = 1-3 of H, halo, cyano, CF3, alkyl, alkoxy; R3 = 1-tetrazolyl or its 5-alkyl or 5-CF3 derivs., 1,2,4-triazol-4-yl, 1H-tetrazol-5-yl; Ar = (un)substituted Ph or pyridyl; A = carboxy- or carboxy-deriv.-substituted pyrrolidino, piperazino, morpholino, thiomorpholino or oxides, or piperidino]. As tachykinin receptor antagonists, the compds. are useful in the treatment of tachykinin-mediated diseases and conditions, including particularly asthma, cough, and bronchitis. For instance, (S)-3-(3,4,5-trimethoxybenzoyl)-3-(3,4-dichlorophenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine was condensed with 4-phenyl-4-[[(S)-2-carbomethoxypyrrolidin-1-yl]carboxamido]piperidine hydriodide to give title compd. II. The latter bound to NK1 and NK2 receptors in vitro with IC50 values of 4.32 nM and 4.51 nM, resp.

IT **40878-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of heterocyclic carboxy-substituted cyclic carboxamide derivs. as tachykinin receptor antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)

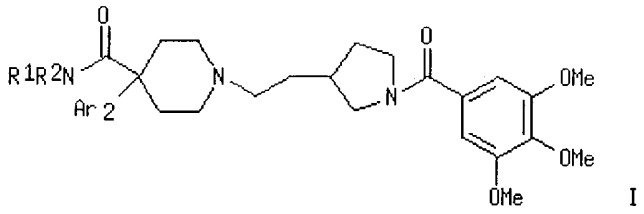


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:723316 HCAPLUS
DOCUMENT NUMBER: 128:34664
TITLE: Synthesis and structure-activity relationships for a series of substituted pyrrolidine NK1/NK2 receptor antagonists
AUTHOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Maynard, George D.; Liu, Xiao-Gao; Le, Tieu-Binh; Webster, Mark E.; Horgan, Stephen W.; Wenstrup, David L.; Freund, David W.; Boyer, Fred; Bratton, Larry; Gross, Raymond S.; Knippenberg, Robert W.; Logan, Deborah E.; Jones, Bryan K.; Chen, Teng-Man; Geary, Julie L.; Correll, Melinda A.; Poole, J. Chuck; Mandagere, Arun K.; Thompson, Thomas N.; Hwang, Kin-Kai
CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(19), 2531-2536
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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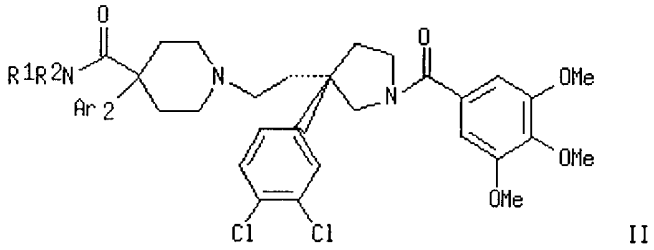


II

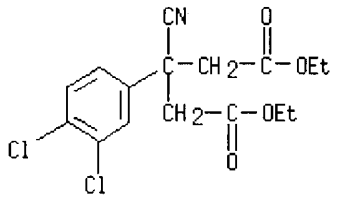
AB The authors recently described the synthesis and characterization of MDL 105,212, a non peptide tachykinin antagonist with high affinity for NK1 and NK2 receptors. Here, the authors report the synthesis and structure-activity relationships for a series of analogs of MDL 105,212, I (Ar1 = 3-ClC6H4, 4-FC6H4, 3-pyridyl, etc., Ar2 = Ph, 3-MeOC6H4, 4-FC6H4, 3-, 4-pyridyl, R1R2N, = H2N, piperidino, morpholino, 4-methylpiperidino) and II (Ar2 = Ph, 3-, 4-pyridyl, R1R2N = H2N, morpholino, 4-methylpiperidino), with regards to NK1 and NK2 receptor binding affinity, phys.-chem. characterization; in vitro absorption potential; in vitro metabolic stability; and efficacy in a capsaicin-challenge conscious guinea pig model after oral administration.

IT **40878-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)

(prepn. and structure activity relationship of pyrrolidines as neurokinin receptor antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:618075 HCAPLUS
DOCUMENT NUMBER: 127:278145
TITLE: Preparation of 3-aryl-3-carboxyalkyl glutarimides
INVENTOR(S): Camus, Philippe; Descamps, Marcel; Radisson, Joel
PATENT ASSIGNEE(S): Sanofi, Fr.; Camus, Philippe; Descamps, Marcel; Radisson, Joel
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732852	A1	19970912	WO 1997-FR388	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2745811	A1	19970912	FR 1996-2880	19960307
FR 2745811	B1	19980522		
CA 2244771	AA	19970912	CA 1997-2244771	19970305
AU 9721634	A1	19970922	AU 1997-21634	19970305
EP 888304	A1	19990107	EP 1997-914357	19970305
EP 888304	B1	20011004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506124	T2	19990602	JP 1997-531525	19970305
JP 3116051	B2	20001211		
BR 9707943	A	19990727	BR 1997-7943	19970305
AT 206399	E	20011015	AT 1997-914357	19970305
PT 888304	T	20020228	PT 1997-914357	19970305
ES 2165594	T3	20020316	ES 1997-914357	19970305
TW 381080	B	20000201	TW 1997-86102748	19970306
ZA 9701999	A	19970909	ZA 1997-1999	19970307

US 6008360	A	19991228	US 1998-142306		19980903
NO 9804083	A	19980904	NO 1998-4083		19980904
US 6242607	B1	20010605	US 1999-437362		19991110
PRIORITY APPLN. INFO.:			FR 1996-2880	A	19960307
			WO 1997-FR388	W	19970305
			US 1998-142306	A3	19980903

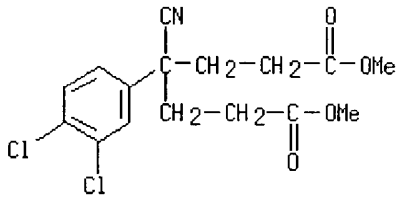
OTHER SOURCE(S): MARPAT 127:278145

AB RCR1R2ZCO2H [I; R = (un)substituted Ph, pyridyl, thienyl; R1R2 = CH2CH2CONHCO; Z = CH2 or CH2CH2] were prepd. by cyclization of I (R1 = cyano, R2 = CH2CH2CN or CH2CH2CO2H).

IT **65619-22-9P**, Dimethyl 4-cyano-4-(3,4-dichlorophenyl)heptanedioate
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of 3-aryl-3-carboxyalkyl glutarimides)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



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L24 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER:	1997:501538 HCAPLUS
DOCUMENT NUMBER:	127:135815
TITLE:	Novel substituted 4-(1H-benzimidazol-2-yl)-[1,4]-diazepanes useful for the treatment of allergic diseases
INVENTOR(S):	Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S):	Hoechst Marion Roussel, Inc., USA
SOURCE:	PCT Int. Appl., 349 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9722604	A1	19970626	WO 1996-US19524	19961204
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2241827	AA	19970626	CA 1996-2241827	19961204
CA 2241827	C	20020430		
AU 9714119	A1	19970714	AU 1997-14119	19961204

AU 707914	B2	19990722			
EP 874843	A1	19981104	EP 1996-944267	19961204	
EP 874843	B1	20020807			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CN 1207097	A	19990203	CN 1996-199141	19961204	
CN 1080262	B	20020306			
BR 9612074	A	19990330	BR 1996-12074	19961204	
JP 2000500772	T2	20000125	JP 1997-522863	19961204	
NZ 325581	A	20000327	NZ 1996-325581	19961204	
AT 221883	E	20020815	AT 1996-944267	19961204	
ES 2177827	T3	20021216	ES 1996-944267	19961204	
PT 874843	T	20021231	PT 1996-944267	19961204	
ZA 9610602	A	19970620	ZA 1996-10602	19961217	
NO 9802867	A	19980819	NO 1998-2867	19980619	
HK 1017684	A1	20021025	HK 1999-102816	19990705	

PRIORITY APPLN. INFO.:

US 1995-580004	A	19951220
US 1996-736411	A	19961024
WO 1996-US19524	W	19961204

OTHER SOURCE(S): MARPAT 127:135815

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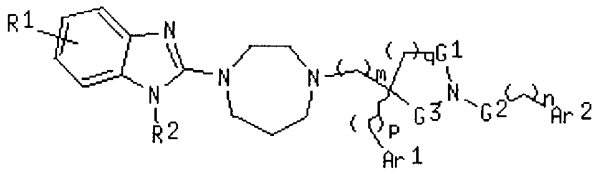

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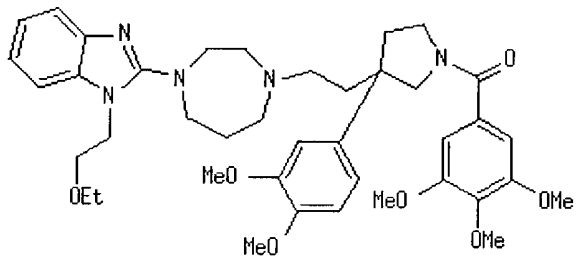


II

AB The invention relates to novel 4-(1H-benzimidazol-2-yl)-[1,4]-diazepane derivs. I and their stereoisomers and pharmaceutically acceptable salts, which are useful as histamine receptor antagonists and tachykinin receptor antagonists (no data) [wherein m = 2, 3; n = 0, 1; q = 1, 2; p = 0, 1; G1 = CH2, CO; G2 = CH2, CHMe, CO; G3 = CH2, CO; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, 3,4-methylenedioxy- or 3,4-ethylenedioxyphenyl; R1 = H, halo, CF3, alkyl, alkoxy; R2 = H, certain (un)substituted alkyl or alkenyl, etc.]. Such antagonists are useful in the treatment of allergic rhinitis, including seasonal rhinitis and sinusitis, inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, asthma, bronchitis, and emesis. Over 90 synthetic examples are given. For instance, 3-(3,4-dimethoxyphenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) underwent a sequence of amidation with 3,4,5-trimethoxybenzoyl chloride, conversion to the mesylate ester, and condensation of the mesylate with the corresponding diazepane deriv., to give title compd. II.

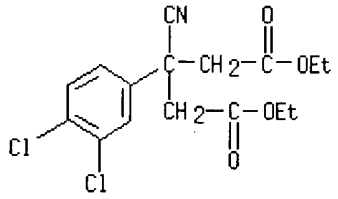
IT **40878-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)

(intermediate; prepn. of benzimidazolyldiazepanes as antiallergics and antiinflammatories)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:453985 HCAPLUS
DOCUMENT NUMBER: 127:81450
TITLE: Substituted 4-(1H-benzimidazol-2-ylamino)piperidines useful for the treatment of allergic diseases
INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: PCT Int. Appl., 323 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719074	A1	19970529	WO 1996-US18001	19961107
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2000500742	T2	20000125	JP 1997-517638	19961030
CA 2237971	AA	19970529	CA 1996-2237971	19961107
CA 2237971	C	20020122		
AU 9710508	A1	19970611	AU 1997-10508	19961107
AU 703701	B2	19990401		
CN 1202894	A	19981223	CN 1996-198360	19961107
CN 1098264	B	20030108		
EP 920425	A1	19990609	EP 1996-941334	19961107
EP 920425	B1	20030219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11513991	T2	19991130	JP 1997-519767	19961107
IL 124396	A1	20010319	IL 1996-124396	19961107
AT 232858	E	20030315	AT 1996-941334	19961107
ES 2188801	T3	20030701	ES 1996-941334	19961107
PT 920425	T	20030731	PT 1996-941334	19961107

ZA 9609484	A	19970610	ZA 1996-9484		19961112
TW 394771	B	20000621	TW 1996-85115760		19961220
NO 9802238	A	19980701	NO 1998-2238		19980515
HK 1018065	A1	20030606	HK 1999-103106		19990720
PRIORITY APPLN. INFO.:			US 1995-560419	A	19951117
			US 1996-734508	A	19961017
			US 1995-8108P	P	19951030
			US 1995-7473P	P	19951122
			US 1995-8992P	P	19951221
			US 1996-13747P	P	19960320
			US 1996-13748P	P	19960320
			US 1996-13764P	P	19960320
			US 1996-17455P	P	19960517
			US 1996-17892P	P	19960517
			US 1996-22047P	P	19960722
			US 1996-23494P	P	19960907
			WO 1996-US18001	W	19961107

OTHER SOURCE(S): MARPAT 127:81450

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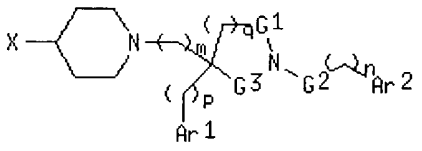

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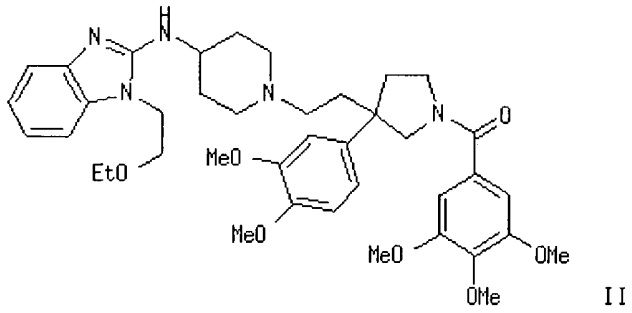


II

AB The invention relates to novel substituted piperidine derivs. I [m = 2, 3; n = 0, 1; q = 1, 2; p = 0, 1; G1 = CH2, CO; G2 = CH2, CHMe, CO; G3 = CH2, CO; Ar1 = (un)substituted Ph, naphthyl, pyridyl, or thienyl; Ar2 = (un)substituted Ph, benzodioxol-5-yl, benzodioxan-6-yl; X = (un)substituted benzimidazol-2-ylamino; with several provisos] and their stereoisomers and pharmaceutically acceptable salts. The compds. are useful as histamine receptor antagonists and tachykinin receptor antagonists (no data). Such antagonists are useful in the treatment of allergic rhinitis, including seasonal rhinitis and sinusitis, inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, asthma, bronchitis, and emesis. For example, 3-(3,4-dimethoxyphenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) underwent amidation with 3,4,5-trimethoxybenzoyl chloride, followed by mesylation with MeSO2Cl and Et3N, and coupling with [1-(2-ethoxyethyl)-1H-benzimidazol-2-yl](piperidin-4-yl)amine (prepn. given), to give title compd. II.

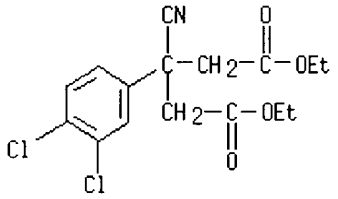
IT **40878-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)

(intermediate; prepn. of (benzimidazolylamino)piperidines as antiallergics)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:375289 HCAPLUS
DOCUMENT NUMBER: 127:95200
TITLE: Substituted pyrrolidin-3-yl-alkyl-piperidines useful as tachykinin antagonists
INVENTOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Maynard, George D.
PATENT ASSIGNEE(S): Merrell Pharmaceuticals Inc., USA
SOURCE: U.S., 82 pp., Cont.-in-part of U.S. Ser. No. 225,371, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5635510	A	19970603	US 1994-332027	19941031
CN 1124961	A	19960619	CN 1994-192362	19940422
CN 1081635	B	20020327		
ZA 9403091	A	19950112	ZA 1994-3091	19940504
US 5648366	A	19970715	US 1995-477167	19950607
US 5861416	A	19990119	US 1997-795576	19970206
US 5824690	A	19981020	US 1997-798664	19970211

PRIORITY APPLN. INFO.: US 1993-58606 B2 19930506
US 1994-225371 B2 19940419
US 1994-332027 A3 19941031

OTHER SOURCE(S): MARPAT 127:95200
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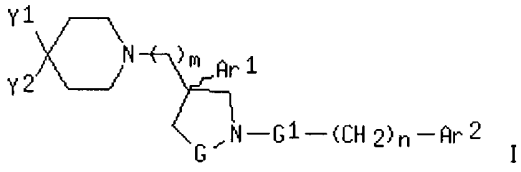

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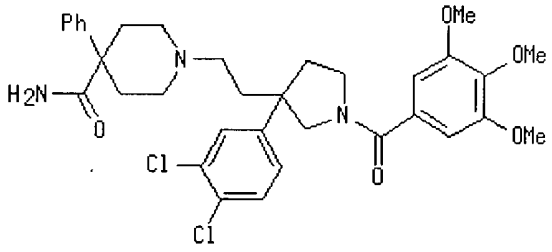


II

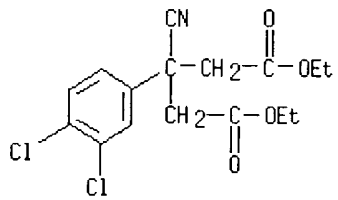
AB The invention relates to substituted pyrrolidinyl-3-yl-alkyl-piperidines I [G, G1 = CH2, CO; m = 2, 3; n = 0, 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl, or benzo[1,3]dioxan-5-yl; Ar2 = (un)substituted Ph or pyridyl; Y1 = (un)substituted CONH2; Y2 = (un)substituted Ph, naphthyl, pyridyl, thienyl, or CH2Ph; or Y1Y2 = atoms to complete certain Ph-substituted, 5-membered, diazaspiro ring fusions], their stereoisomers, N-oxides, and pharmaceutically acceptable salts, and processes for prepn. of the same. I are useful for their pharmacol. activities, such as tachykinin antagonism, and esp. substance P and neurokinin A antagonism. Such compds. are indicated for conditions assocd. with neurogenic inflammation and other diseases. For instance, 3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)pyrrolidine underwent a sequence of amidation with 3,4,5-trimethoxybenzoyl chloride (71%), conversion of the alc. to a methanesulfonate ester (92%), and reaction of the mesylate moiety with 4-phenylpiperidine-4-carboxamide-HCl (71%), to give title compd. II. In an assay for modulation of NKA-induced respiratory effects in guinea pigs, II at 10 mg/kg reduced dyspnea to 60% of control.

IT **40878-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of pyrrolidinylalkylpiperidines as tachykinin antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing... References

ACCESSION NUMBER: 1997:302959 HCAPLUS
DOCUMENT NUMBER: 126:277403
TITLE: Novel human NK3 receptor-selective antagonist compounds containing them

INVENTOR(S): Bichon, Daniel; Edmonds-Alt, Xavier; Gueule, Patrick; Proietto, Vincenzo; Van Broeck, Didier

PATENT ASSIGNEE(S): Sanofi, Fr.; Bichon, Daniel; Edmonds-Alt, Xavier; Gueule, Patrick; Proietto, Vincenzo; Van Broeck, Didier

SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9710211	A1	19970320	WO 1996-FR1416	19960913
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
FR 2738819	A1	19970321	FR 1995-10776	19950914
FR 2738819	B1	19971205		
CA 2232007	AA	19970320	CA 1996-2232007	19960913
AU 9669925	A1	19970401	AU 1996-69925	19960913
BR 9610081	A	19990105	BR 1996-10081	19960913
JP 11514983	T2	19991221	JP 1997-511718	19960913
EP 1019373	A1	20000719	EP 1996-931126	19960913
EP 1019373	B1	20031112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1241168	A1	20020918	EP 2002-10824	19960913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 254104	E	20031115	AT 1996-931126	19960913
US 6028082	A	20000222	US 1998-43247	19980312
US 6291672	B1	20010918	US 1999-437203	19991109
US 2002049329	A1	20020425	US 2001-954862	20010918
US 6710042	B2	20040323		

PRIORITY APPLN. INFO.:

FR 1995-10776	A	19950914
EP 1996-931126	A3	19960913
WO 1996-FR1416	W	19960913
US 1998-43247	A3	19980312

OTHER SOURCE(S): MARPAT 126:277403

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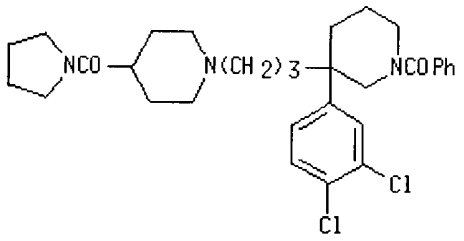


I

AB Piperidinopropylpiperidine derivs. were prepd. for use as human NK3 receptor antagonists (no data). Thus, 3,4-Cl2C6H3CH2CN was treated with

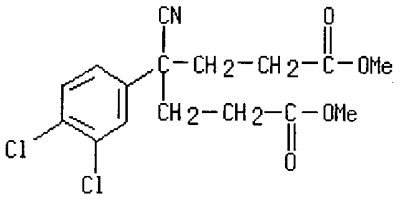
CH2:CHCO2Me to give 3,4-Cl2C6H3CH(CN)(CH2CH2CO2Me)2 which was cyclized to the piperidonepropanoate and reduced to 3-(3,4-dichlorophenyl)-3-(3-hydroxypropyl)piperidine (I). I was N-benzoylated, converted to the mesylate, and aminated to give the piperidinopropylpiperidine II.

IT **65619-22-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of piperidinopropylpiperidines as NK3 antagonists)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:544033 HCAPLUS
DOCUMENT NUMBER: 125:195439
TITLE: Heterocyclic compounds as tachykinin receptor antagonists, process for their preparation, and pharmaceuticals containing them
INVENTOR(S): Emonds-Alt, Xavier; Grossriether, Isabelle; Proietto, Vincenzo; Van Broeck, Didier
PATENT ASSIGNEE(S): Sanofi, Fr.
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 723959	A1	19960731	EP 1996-400202	19960129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2729951	A1	19960802	FR 1995-1015	19950130
FR 2729951	B1	19970418		
EP 1101757	A1	20010523	EP 2001-100819	19960129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 08245622	A2	19960924	JP 1996-14703	19960130
US 5656639	A	19970812	US 1996-593929	19960130
US 5859029	A	19990112	US 1997-787910	19970123

PRIORITY APPLN. INFO.:

FR 1995-1015	A	19950130
EP 1996-400202	A3	19960129
US 1996-593929	A3	19960130

OTHER SOURCE(S): MARPAT 125:195439
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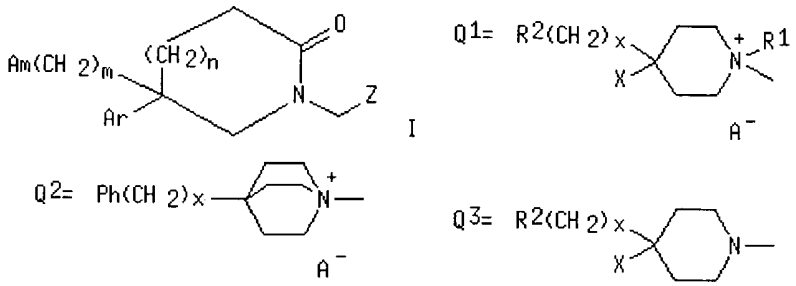

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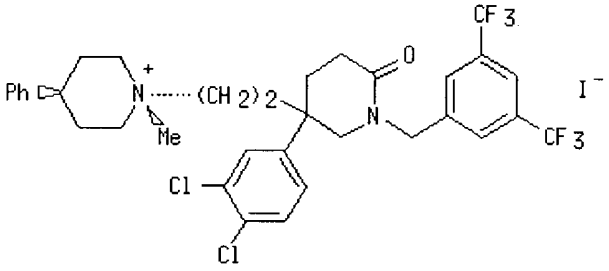


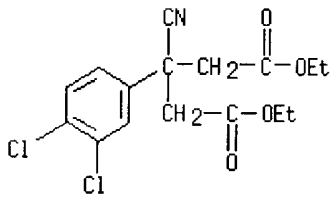
II

AB Title compds. I [m = 2, 3; n = 0, 1, 2; Am = piperidinium group Q1, quinuclidinium group Q2, and (when n = 0) piperidine group Q3; R1 = alkyl, benzyl; R2 = (un)substituted Ph; X = H, OH; x = 0, 1; Ar = (halo)phenyl, naphthyl, indolyl; Z = Ph optionally substituted by halo, alkyl, or CF3; A- = anion] and their acid salts and solvates are claimed. The compds. have a strong affinity for NK1 receptors, and are useful for treatment of substance P-mediated pathologies, such as pain, allergy, inflammation, etc. For example, 4-phenylpiperidine was N-alkylated by 5-[2-(mesyloxy)ethyl]-5-(3,4-dichlorophenyl)-1-[3,5-bis(trifluoromethyl)benzyl]piperid-2-one [prepn. given], followed by quaternization with MeI to give the axial-Me-isomeric title compd. II, plus its equatorial-Me isomer. In a test for inhibition of substance P binding at human lymphoblastic receptors, II had a Ki on the order of 0.1 × 10-9 M, whereas a similar known compd. from EP-0512901 had Ki of only approx. 10-6 M.

IT **40878-10-2P**, Diethyl 3-cyano-3-(3,4-dichlorophenyl)-1,5-pentanedioate
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of quinuclidinium and piperidine derivs. as tachykinin receptor antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:404635 HCAPLUS

DOCUMENT NUMBER: 125:114615
TITLE: 1-Benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivatives and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases
INVENTOR(S): Burkholder, Timothy P.; Bratton, Larry D.; Kudlacz, Elizabeth M.; Maynard, George D.; Kane, John M.; Santiago, Braulio
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 294 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606094	A1	19960229	WO 1995-US10640	19950817
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2198084	AA	19960229	CA 1995-2198084	19950817
AU 9534928	A1	19960314	AU 1995-34928	19950817
AU 693936	B2	19980709		
EP 777666	A1	19970611	EP 1995-931551	19950817
EP 777666	B1	19990303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1158612	A	19970903	CN 1995-195283	19950817
CN 1067385	B	20010620		
HU 76644	A2	19971028	HU 1997-1257	19950817
HU 221434	B	20021028		
JP 10504580	T2	19980506	JP 1995-508257	19950817
AT 177095	E	19990315	AT 1995-931551	19950817
ES 2132709	T3	19990816	ES 1995-931551	19950817
ZA 9507033	A	19960416	ZA 1995-7033	19950822
IL 115040	A1	20000229	IL 1995-115040	19950823
TW 430663	B	20010421	TW 1995-84108797	19950823
FI 9700771	A	19970224	FI 1997-771	19970224
NO 9700831	A	19970418	NO 1997-831	19970224

PRIORITY APPLN. INFO.: US 1994-295960 A 19940825
US 1995-501914 A 19950713
WO 1995-US10640 W 19950817

OTHER SOURCE(S): MARPAT 125:114615
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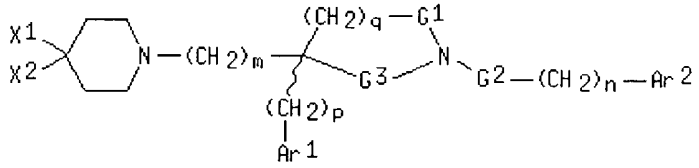

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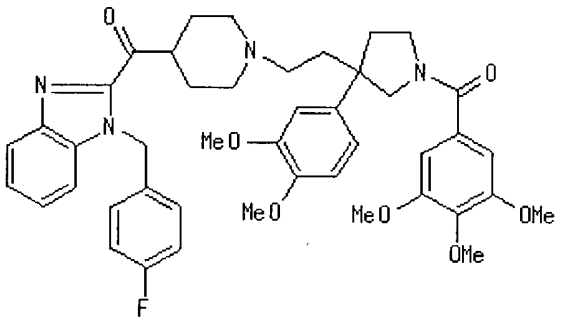


II

AB The present invention relates to novel substituted piperidine derivs. I wherein: G1 is CH2 or CO; G2 is CH2 or CO; G3 is CH2 or CO; m is 2 or 3; n is 0 or 1; q is 1 or 2; p is 0 or 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, pyridyl; X1 and X2 are defined in one of (A), (B), or (C): (A) X1 = H and X2 = substituted benzothiazole-2-carbonyl, diphenylmethyl, benzimidazolyl-2-carbonyl; (B) X1 = OH and X2 = substituted benzothiazol-2-yl, benzimidazol-2-yl; (C) X2 = (R5C6H4)C(Z1)(C6H4R6) wherein R5, R6 = from 1 to 3 substituents chosen independently from, e.g., H, halo, CF3, and X1 and Z1 taken together form a second bond between the carbon atoms bearing X1 and Z1; provided than when G1 is CO, then G2 and G3 are CH2, and that when G2 is CO, then G1 and G3 are CH2, and that when G3 is CO, then G1 and G2 are CH2; stereoisomers thereof, and pharmaceutically acceptable salts thereof which are useful as histamine receptor antagonists and tachykinin receptor antagonists. Such antagonists are useful in the treatment of allergic diseases including: seasonal rhinitis, allergic rhinitis, and sinusitis. Thus, e.g., substitution reaction of 4-[1-(4-fluorobenzyl)-1H-benzimidazole-2-carbonyl]piperidine with 1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine (prepn. given) afforded II which exhibited H1 receptor antagonism in vitro with pA2 = 7.50, and NK1 receptor binding affinity with IC50 = 31 nM.

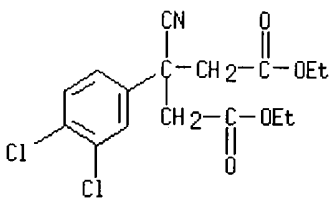
IT **40878-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)

(1-benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivs. and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)

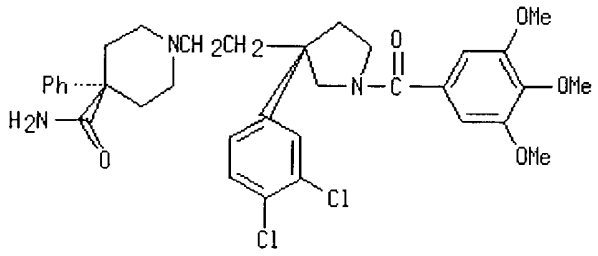


L24 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:288884 HCAPLUS
DOCUMENT NUMBER: 125:33442
TITLE: Identification and chemical synthesis of MDL 105,212, a non-peptide tachykinin antagonist with high affinity for NK1 and NK2 receptors
AUTHOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Le, Tieu-Binh; Knippenberg, Robert W.; Shatzer, Scott A.; Maynard, George D.; Webster, Mark E.; Horgan, Stephen W.
CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(8), 951-956
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

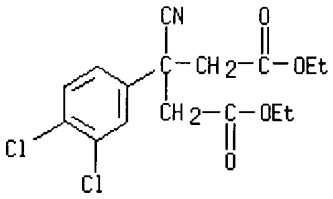
103 (a)



I

AB A nonpeptide tachykinin receptor antagonist 105,212 (I) was identified that has high affinity for human NK1 (IC50 = 3.11 nM) and NK2 (IC50 = 8.40 nM) receptors. The chem. synthesis of MDL 105212 and the structure-activity relationship of a series of racemic amide analogs are described.

IT **40878-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of MDL 105212 non-peptide tachykinin antagonist)
RN 40878-10-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:994586 HCAPLUS
DOCUMENT NUMBER: 124:117093
TITLE: Preparation of N-[(3,4-dichlorophenyl)propyl]piperidine selective human NK3-receptor antagonists

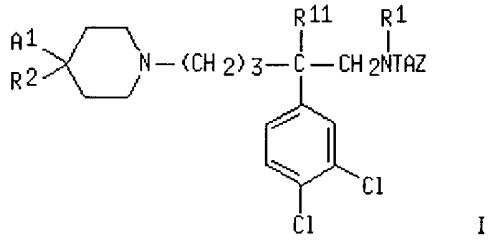
INVENTOR(S): Bichon, Daniel; Van, Broeck Didier; Proietto, Vincenzo; Gueule, Patrick; Emonds-Alt, Xavier
PATENT ASSIGNEE(S): SANOFI, Fr.
SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 673928	A1	19950927	EP 1995-400590	19950317
EP 673928	B1	20010829		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2717477	A1	19950922	FR 1994-3193	19940318
FR 2717477	B1	19960607		
FR 2717478	A1	19950922	FR 1994-9478	19940729
FR 2717478	B1	19960621		
FR 2719311	A1	19951103	FR 1995-571	19950119
FR 2719311	B1	19980626		
PL 185075	B1	20030228	PL 1995-307723	19950316
FI 9501265	A	19950919	FI 1995-1265	19950317
NO 9501044	A	19950919	NO 1995-1044	19950317
AU 9514909	A1	19950928	AU 1995-14909	19950317
AU 693845	B2	19980709		
ZA 9502228	A	19951221	ZA 1995-2228	19950317
HU 72065	A2	19960328	HU 1995-806	19950317
CN 1128756	A	19960814	CN 1995-103542	19950317
CN 1056605	B	20000920		
IL 113026	A1	19990620	IL 1995-113026	19950317
RU 2143425	C1	19991227	RU 1995-103737	19950317
AT 204863	E	20010915	AT 1995-400590	19950317
PT 673928	T	20020228	PT 1995-400590	19950317
ES 2164746	T3	20020301	ES 1995-400590	19950317
TW 380138	B	20000121	TW 1995-84102614	19950318
CA 2145000	AA	19950919	CA 1995-2145000	19950320
CA 2145000	C	20020507		
JP 08048669	A2	19960220	JP 1995-61419	19950320
JP 2922816	B2	19990726		
US 5741910	A	19980421	US 1996-607976	19960229
US 5942523	A	19990824	US 1996-608718	19960229
NO 9705089	A	19950919	NO 1997-5089	19971104
HK 1005137	A1	20020315	HK 1998-104342	19980519
US 6124316	A	20000926	US 1999-306825	19990507
US 6294537	B1	20010925	US 1999-306821	19990507

PRIORITY APPLN. INFO.:

FR 1994-3193	A	19940318
FR 1994-9478	A	19940729
FR 1995-571	A	19950119
US 1995-405833	A3	19950317
US 1997-880832	B1	19970623

OTHER SOURCE(S): MARPAT 124:117093
GI



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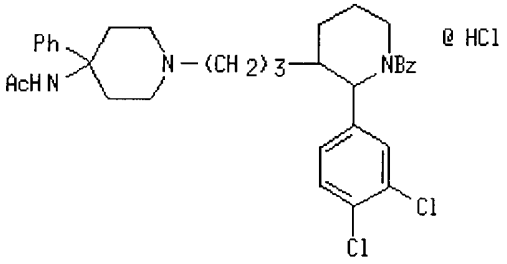


II

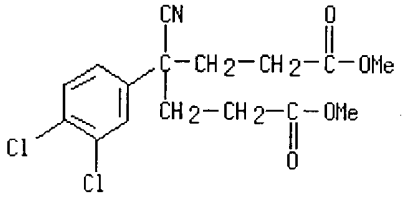
AB The title compds. [I; A = direct bond, CH2, CH2CH2, CH:CH; A1 = (un)substituted 2-pyridyl or Ph; R1 = Me; R2 = HO, alkoxy, CN, (un)substituted NH2, etc.; R11 = H; such that R1R11 = (CH2)3] (e.g., II; m.p. 184°), useful as human NK3-receptor antagonists (no data) for the treatment of neurokinin B-induced diseases (no data), are prepd.

IT **65619-22-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of N-[(3,4-dichlorophenyl)propyl]piperidine selective human NK3-receptor antagonists from)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



108(a)

L24 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:772578 HCAPLUS
DOCUMENT NUMBER: 123:198629
TITLE: Preparation of substituted (pyrrolidin-3-ylalkyl)piperidines as tachykinin antagonists
INVENTOR(S): Burkholder, Timothy P.; Le, Tieu-Binh; Kudlacz, Elizabeth M.; Maynard, George D.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 238 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

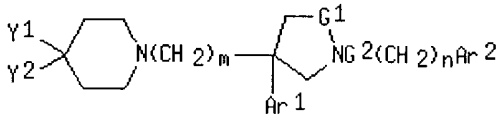
WO 9426735	A1	19941124	WO 1994-US4498	19940422
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2160462	AA	19941124	CA 1994-2160462	19940422
CA 2160462	C	19981215		
AU 9469426	A1	19941212	AU 1994-69426	19940422
AU 678023	B2	19970515		
EP 696280	A1	19960214	EP 1994-917898	19940422
EP 696280	B1	19970924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 74085	A2	19961128	HU 1995-3153	19940422
JP 09500361	T2	19970114	JP 1994-525453	19940422
JP 3424174	B2	20030707		
AT 158580	E	19971015	AT 1994-917898	19940422
ES 2110761	T3	19980216	ES 1994-917898	19940422
IL 109496	A1	20000726	IL 1994-109496	19940502
ZA 9403091	A	19950112	ZA 1994-3091	19940504
FI 9505258	A	19951130	FI 1995-5258	19951102
NO 9504400	A	19960108	NO 1995-4400	19951103

PRIORITY APPLN. INFO.:

US 1993-58606	A	19930506
US 1994-218483	A	19940328
US 1994-225371	A	19940419
WO 1994-US4498	W	19940422

OTHER SOURCE(S): MARPAT 123:198629

GI



I

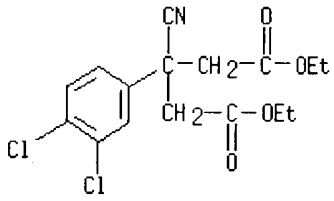
AB Title compds. I (G1, G2 = CH2, CO; m = 2,3; n = 0,1; Ar1, Y2 = (substituted)aryl, (substituted)heterocyclyl; Ar2 = (substituted)Ph or heterocyclyl; Y1 = (substituted)HNCO, (dialkylamino)carbonyl, N-heterocyclylcarbonyl; Y1Y2 together with the C to which they are attached form a substituted spirocyclyl), or stereoisomers, or salts thereof, are prepd. I are claimed for treatment of neurogenic inflammatory diseases, asthma, pain, and cough. 3-(3,4-Dichlorophenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) was reacted with 2,4-dimethoxybenzoyl chloride to give 3-(3,4-dichlorophenyl)-1-(2,4-dimethoxybenzoyl)-3-(2-hydroxyethyl)pyrrolidine which in 2 steps was converted to I (G1 = H2C, G2 = CO, m = 2, n = 0, Ar1 = 3,4-Cl2C6H3, Ar2 = 2,4-(MeO)2C6H3, Y1 = H2NCO, Y2 = Ph). Tachykinin antagonism was demonstrated.

IT **40878-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of substituted (pyrrolidinylalkyl)piperidines as tachykinin antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1982:34690 HCAPLUS
DOCUMENT NUMBER: 96:34690
TITLE: 4-Amino-4-arylcyclohexanones and their ketals
INVENTOR(S): Lednicer, Daniel
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: Can., 184 pp.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1100516	A2	19810505	CA 1980-352654	19800523
US 4065573	A	19771227	US 1976-692589	19760603
CA 1093553	A1	19810113	CA 1977-278494	19770516
IL 59312	A1	19840131	IL 1977-59312	19770520
US 4460604	A	19840717	US 1980-199415	19801022

PRIORITY APPLN. INFO.:

US 1976-692589	19760603
CA 1977-278494	19770516
IL 1977-52131	19770520
US 1977-840861	19771011
US 1979-23921	19790326

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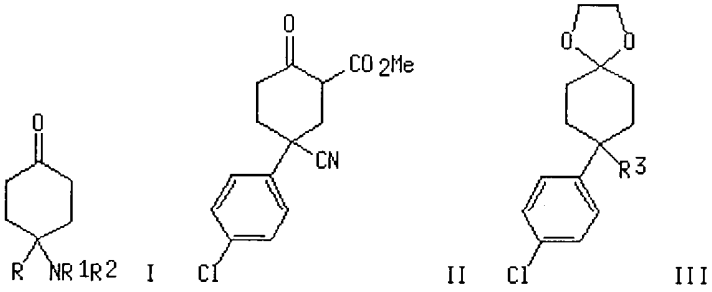


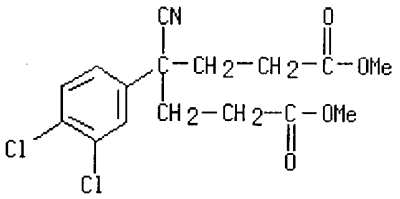
AB Aminocyclohexanones I [R = thiopheno, (un)substituted Ph or arylalkoxy; R1 = C1-8 alkyl; R2 = C1-8 alkyl, C4-9 cycloalkylalkyl, C3-6 cycloalkyl, arylalkyl, aryloxyalkyl, alkoxy] (~230 compds.) were prepd. as analgesics (no data), e.g. from benzeneacetonitriles. Thus, adding 4-ClC6H4CH2CN to CH2:CHCO2Me in Me3COH gave (4-ClC6H4)(NC)C(CH2CH2CO2Me)2, which was cyclized with KOCMe3 to II whose decarboxylation and ketalization gave III (R3 = cyano). The last was hydrolyzed to the acid, converted into the isocyanate with Ph2P(O)N3, reduced with LiAlH4, and

methylated with HCHO-NaBH4 to give III (R3 = NMe2).

IT 65619-22-9P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1982:19734 HCAPLUS
DOCUMENT NUMBER: 96:19734
TITLE: 4-Amino-4-arylcyclohexanone ketals
INVENTOR(S): Lednicer, Daniel
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: Can., 185 pp. Division of Can. Appl. No. 278,494.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1105938	A2	19810728	CA 1980-359623	19800905
US 4065573	A	19771227	US 1976-692589	19760603
CA 1093553	A1	19810113	CA 1977-278494	19770516
IL 59312	A1	19840131	IL 1977-59312	19770520
US 4460604	A	19840717	US 1980-199415	19801022

PRIORITY APPLN. INFO.:

US 1976-692589	19760603
CA 1977-278494	19770516
IL 1977-52131	19770520
US 1977-840861	19771011
US 1979-23921	19790326

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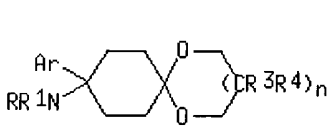

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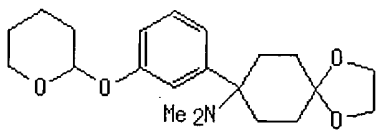


II

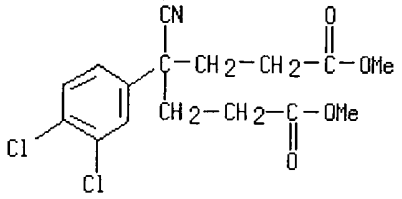
AB I [Ar = [(tetrahydro-2H-pyran-2-yl)oxy]phenyl; R = C1-8 alkyl; R1 = C1-8 alkyl, C3-6 cycloalkyl [(C3-6-cycloalkyl)C1-3-alkyl], Rx2C6H5-xCH2, Rx2C6H5-xCH2CH2, Rx2C6H5-xOCH2CH2 (R2 = halo, CF3, C1-4 alkyl, C1-4 alkoxy; x = 0-2); n = 0 or 1; R3 = H or Me; R4 = H, Ph, alkenyl] were prepd. as analgesics (no data). Thus, 4-cyano-4-(dimethylamino)cyclohexanone cyclic ethylene ketal was treated with the

Grignard reagent from 2-(3-bromophenoxy)tetrahydro-2H-pyran to give II.

IT **65619-22-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 65619-22-9 HCAPLUS

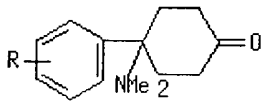
CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1980:180773 HCAPLUS
DOCUMENT NUMBER: 92:180773
TITLE: 4-Amino-4-arylcyclohexanones and their derivatives, a novel class of analgesics. 1. Modification of the aryl ring
AUTHOR(S): Lednicer, Daniel; Von Voigtlander, Philip F.; Emmert, D. Edward
CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of Medicinal Chemistry (1980), 23(4), 424-30
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 92:180773
GI



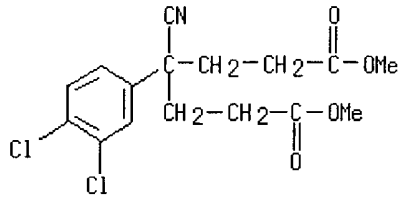
I

AB Synthesis of title compds. (I) involved double Michael reaction of Me acrylate with arylacetonitriles, followed by cyclization, decarboxylation, ketalization, and sapon.; the geminally substituted acid formed was rearranged to the isocyanate with (PhO)2PON3, and the isocyanates were converted into I via LiAlH4 redn. and methylation with CH2O. Analgesic activity was very sensitive to the nature and position of the substituent on the arom. ring. The most potent compds. in this series (I, R = 4-Me, 4-Br) showed 50% the potency of morphine. Deletion of the ring oxygen abolished activity.

IT **65619-22-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1978:104776 HCAPLUS
DOCUMENT NUMBER: 88:104776
TITLE: 4-Amino-4-arylcyclohexanone compounds and intermediates
INVENTOR(S): Lednicer, Daniel
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: Ger. Offen., 273 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2723937	A1	19771215	DE 1977-2723937	19770526
US 4065573	A	19771227	US 1976-692589	19760603
ZA 7702819	A	19780726	ZA 1977-2819	19770511
IL 52131	A1	19840131	IL 1977-52131	19770520
IL 59312	A1	19840131	IL 1977-59312	19770520
AU 7725425	A1	19781130	AU 1977-25425	19770524
AU 511781	B2	19800904		
NL 7706051	A	19771206	NL 1977-6051	19770602
FR 2354992	A1	19780113	FR 1977-16901	19770602
ES 459429	A1	19781116	ES 1977-459429	19770602
GB 1561205	A	19800213	GB 1977-23366	19770602
GB 1561206	A	19800213	GB 1978-35783	19770602
BE 855405	A1	19771205	BE 1977-178211	19770603
JP 53018546	A2	19780220	JP 1977-65685	19770603
US 4180584	A	19791225	US 1977-840861	19771011
US 4460604	A	19840717	US 1980-199415	19801022

PRIORITY APPLN. INFO.:

US 1976-692589	19760603
IL 1977-52131	19770520
US 1977-840861	19771011
US 1979-23921	19790326

OTHER SOURCE(S): CASREACT 88:104776
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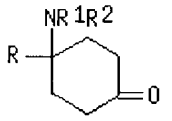

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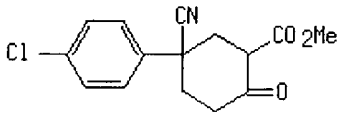

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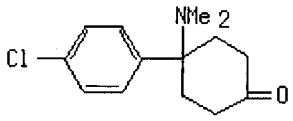


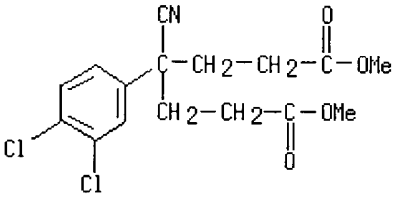
III

AB The title compds. (~200) I (R = thienyl, naphthyl, Ph, or substituted aryl; R1, R2 = Me, allyl, pentyl, Bu, etc.) and/or their cyclic ketals, useful as analgesics and narcotic antagonists, were prepd. Thus, 4-ClC6H4CH2CN with 2 mol. CH2:CHCO2Me followed by cyclization gave II, which on hydrolysis-decarboxylation, ketalization with HOCH2CH2OH, hydrolysis of the CN group to CO2H, conversion of the CO2H to isocyanato (by Ph3PN3), redn. of the isocyanate to NHMe, N-methylation, and hydrolysis of the ketal group gave III.

IT **65619-22-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1974:146010 HCAPLUS
DOCUMENT NUMBER: 80:146010
TITLE: 1-Pyrrolidinylbutyrophenone derivatives
INVENTOR(S): Bastian, Jean M.; Strasser, Michael
PATENT ASSIGNEE(S): Sandoz Ltd.
SOURCE: Ger. Offen., 65 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2345192	A1	19740328	DE 1973-2345192	19730907
NL 7312262	A	19740313	NL 1973-12262	19730906
US 3903111	A	19750902	US 1973-394685	19730906
GB 1440380	A	19760623	GB 1973-41914	19730906
BE 804701	A1	19740311	BE 1973-135531	19730910
JP 49069661	A2	19740705	JP 1973-101293	19730910
DD 108533	C	19740920	DD 1973-173381	19730910

AU 7360170	A1	19750313	AU 1973-60170	19730910
HU 167372	P	19750927	HU 1973-SA2530	19730910
ES 418619	A1	19760601	ES 1973-418619	19730910
AT 7307802	A	19770215	AT 1973-7802	19730910
SU 548206	D	19770225	SU 1973-1957934	19730910
FR 2198756	A1	19740405	FR 1973-32612	19730911
ZA 7307236	A	19750430	ZA 1973-7236	19730911

PRIORITY APPLN. INFO.: CH 1972-13280 19720911
CH 1972-16930 19721121

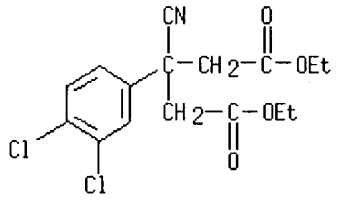
GI For diagram(s), see printed CA Issue.

AB Analgesic pyrrolidinylbutyrophenones I (R = Ph, substituted phenyl; R1 = H, Me, Et, Ac, COEt, COCMe3, CONHMe; n = 1, 2) and some related compds. (40 compds.) were prepd. Thus CH2(CO2Et)2, treated with PhCHO gave the PhCH:C(CO2Et)2 which was treated with KCN in EtOH to give NCCHPhCH2CO2Et (II). Reaction of II with BrCH2CO2Et gave NCCPh(CH2CO2Et)2 (III). Reductive cyclization of III gave Et 3-phenyl-5-oxopyrrolidine-3-acetate, which was successively hydrolyzed to the acid, reduced to the alc. with LiAlH4 and treated with Cl(CH2)3COC6H4F-p to give I (R = Ph, R1 = H, n = 2).

IT **40878-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and reductive cyclization of)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1973:159422 HCAPLUS
DOCUMENT NUMBER: 78:159422
TITLE: Spiro heterocyclics
INVENTOR(S): Bastian, Jean Michel; Hasspacher, Klaus; Strasser, Michael
PATENT ASSIGNEE(S): Sandoz Ltd.
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2241027	A1	19730301	DE 1972-2241027	19720821
CH 556835	A	19741213	CH 1971-12318	19710823
ES 406008	A1	19760601	ES 1972-406008	19720421
SE 385584	B	19760712	SE 1972-10502	19720814
NL 7211304	A	19730227	NL 1972-11304	19720818
FR 2150797	A1	19730413	FR 1972-29540	19720818

BE 787804	A1	19730221	BE 1972-121173	19720821
PL 79446	P	19750630	PL 1972-157376	19720821
GB 1401048	A	19750723	GB 1972-38802	19720821
GB 1401049	A	19750723	GB 1975-4517	19720821
JP 48029765	A2	19730419	JP 1972-84027	19720822
HU 165127	P	19740628	HU 1972-SA2388	19720822
AT 7207228	A	19750915	AT 1972-7228	19720822
AT 330167	B	19760625		
DD 102146	C	19731212	DD 1972-165200	19720823
AU 7245897	A1	19740228	AU 1972-45897	19720823
ZA 7205796	A	19740424	ZA 1972-5796	19720823
ZA 7400329	A	19740529	ZA 1974-329	19720823
US 3901916	A	19750826	US 1973-419670	19731128
AT 7406072	A	19750915	AT 1974-6072	19740724

PRIORITY APPLN. INFO.:

CH 1971-12318	19710823
US 1972-282609	19720821
AT 1972-7228	19720822
CH 1972-17291	19721128

GI For diagram(s), see printed CA Issue.

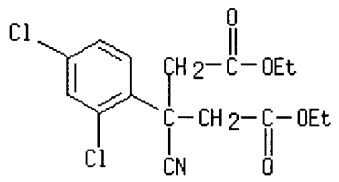
AB Analgesic spiro[indan-1,3'-pyrrolidin]yl-p-fluorobutyrophenones I (R = H, R1 = H, 6-MeO, 6-Cl, 4-Cl, 5-Cl, 4-MeO, 6-Me, 5-F, 5-MeO, 5-Me, 5-Me2CH, 5,7-Cl2, 5,7-Me2, 4,5-Cl2, 5,6-(MeO)2; R = Ac, MeNHCO, EtCO, R1 = H, 5-Cl, 5-Me) were prepd. Thus, PhCHO was treated with CH2-(CO2Et)2 to give PhCH:C(CO2Et)2, which with KCN gave PhCH(CN)CH2CO2Et. The latter was treated with BrCH2CO2Et to give PhC(CN)(CH2CO2Et)2, which was cyclized with Raney Ni to Et 5-oxo-3-phenyl-3-pyrrolidinylacetate. Hydrolysis of the ester to the free acid and cyclization with polyphosphoric acid gave spiro[indan-1,3'-pyrrolidine]-3,5'-dione. LiAlH4 redn. of the ketone yielded spiro[indan-1,3'-pyrrolidin]-3-ol, which on treatment with 2-(3-chloropropyl)-2-(p-fluorophenyl)-1,3-dioxolan or Cl(CH2)3COC6H4F-p gave I (R = R1 = H).

IT **40878-02-2P**

RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 40878-02-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(2,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



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L1 STRUCTURE UPLOADED

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L3 0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4 STRUCTURE UPLOADED

L5 0 S L4

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     FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
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L7             0 S L6
L8             0 S L6 FULL
L9                STRUCTURE UPLOADED
L10            3 S L9
L11           48 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004
L12           69 S L11
L13            1 S L12 AND CASTRO, B?/AU
L14           68 S L12 NOT L13
L15            0 S L14 AND DORMOY, J?/AU
L16            0 S L14 AND RABION, A?/AU

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L17               STRUCTURE UPLOADED
L18            0 S L17
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     FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004
L20           26 S L19
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L22            1 S L20 AND CASTRO, B?/AU
L23            0 S L22 NOT L13
L24           25 S L21 NOT L22

=> s l19
L25          26 L19

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
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FULL ESTIMATED COST                                135.47     774.10

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                -18.02     -18.71

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FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

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  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  This file supports REG1stRY for direct browsing and searching of
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L1              STRUCTURE UPLOADED
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L4              STRUCTURE UPLOADED
L5            0 S L4

     FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
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FILE COVERS 1907 - 16 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 14 May 2004 (20040514/ED)

This file contains CAS Registry Numbers for easy and accurate
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L3 0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004
L4 STRUCTURE UPLOADED
L5 0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004
L6 STRUCTURE UPLOADED
L7 0 S L6
L8 0 S L6 FULL
L9 STRUCTURE UPLOADED
L10 3 S L9
L11 48 S L9 FULL

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L13 1 S L12 AND CASTRO, B?/AU
L14 68 S L12 NOT L13
L15 0 S L14 AND DORMOY, J?/AU
L16 0 S L14 AND RABION, A?/AU

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FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004
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L21 26 S L19/PREP
L22 1 S L20 AND CASTRO, B?/AU
L23 0 S L22 NOT L13
L24 25 S L21 NOT L22
L25 26 S L19

FILE 'CAOLD' ENTERED AT 16:57:59 ON 16 MAY 2004
L26 0 S L19

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                 (L11 (L) THU/RL)

=> s l11/thu
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L28          0 L11/THU
                 (L11 (L) THU/RL)

=> s l11 not l19
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L29         60 L11 NOT L19

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